The New England
Journal of Medicine

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Volume 255 OCTOBER 11, 1956 Number 15

LIGATION OF ESOPHAGEAL VARICES BY THE TRANSABDOMINAL ROUTE*

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THE high mortality among patients who bleed from esophageal varices is well established. Ninety per cent of these patients have a coexisting cirrhosis of the liver as a cause of their portal hypertension and their varices. Approximately two thirds die at the time of their hemorrhage.[1] Stopping the hemorrhage is essential not only because of the danger of exsanguination but also to avoid the metabolic disturbance that follows the absorption of large amounts of blood in the intestine. Many patients exhibit encephalopathies often culminating in coma during bleeding, and their deaths can often be attributed to this complication.[2] Hepatic coma after bleeding from varices into the gastrointestinal tract has been shown to be accompanied by a rise in the value for ammonia nitrogen in the blood and may be more rightly called ammonia intoxication. The fact is that the cirrhotic liver cannot metabolize the great amount of protein nitrogen that digestion and absorption of the large amount of blood in the intestinal tract demand. The resulting encephalopathy and coma can be attributed to the high blood ammonia value from all clinical and laboratory evidence although other factors, now unknown, may be simultaneously responsible. Preventing and combating this intoxication of the patient from the digestion and absorption of his own blood is an essential part of treatment. Three major areas of therapeutic attack are open: control of hemorrhage; evacuation of blood from the gastrointestinal tract; and reparative and detoxifying medical therapy.

The first of these items, the control of hemorrhage, is the most essential step since it prevents both death from shock and ammonia intoxication. The tamponade method with a special balloon tube (Sengstaken–Blakemore) is widely used today. This instrument exerts compression on the varices at the cardioesophageal junction, where bleeding usually occurs. Actual surgical ligation of the varices in the esophagus is another measure in more limited use today. Linton and Warren[3] have reported favorably on the value of ligation of esophageal varices performed by the transthoracic approach. The use of the tamponade method alone has been disappointing in my hands. This instrument invariably will stop hemorrhage from varices, but it has been my experience that hemorrhage usually recurs in a few days and that patients do not withstand the vicissitudes of a second hemorrhage even though it is again controlled by intubation. They usually go into coma and die. It is concluded that the tube can be considered only a temporarily useful instrument in the control of hemorrhage. Surgical ligation of the varices is probably the only certain method of immediate control. Crile[4] first described ligation of esophageal varices for the treatment of recurrent bleeding in patients with extrahepatic portal-bed block as a definitive procedure. Linton has reported the use of immediate ligation of esophageal varices in patients bleeding actively. A left-sided thoracotomy is performed, the mediastinum is opened, the esophageal hiatus is enlarged by diaphragmatic incision, the lower esophagus and stomach are opened for 8 to 10 cm., and the varices are oversewn in this procedure. His results with this approach have been good. At the Albany Hospital only 3 transthoracic ligations of varices have been done. In all 3 cases there was considerable blood loss, and the procedure took more time than was desirable for these patients.

Ligation of varices by an abdominal approach seems feasible and has several advantages to recommend it if it can be accomplished. In the first place, celiotomy is technically easier and faster than thoracotomy. It is also performed in an operative field familiar to all surgeons. Celiotomy, furthermore, interferes but little with pulmonary function during operation and in the postoperative period. Finally, this approach through the abdomen has the further advantage of allowing the surgeon to deal with any gastric or duodenal lesion that may be present. When

*Presented at the annual meeting of the New England Surgical Society, Poland Spring, Maine, October 5, 1956.

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Aided by a grant from the United States Public Health Service.

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the diagnosis of the source of bleeding in a given case is in doubt, one hesitates to perform a thoracotomy and esophagotomy. This dilemma is present in patients who have cirrhosis of the liver and a duodenal ulcer. It also is a factor when the presence of varices has not been proved by esophogram or esophagoscopy. Everyone will agree that to be able to cover several contingencies in these severely ill patients by one approach has something to offer. It should be emphasized now that ligation of esophageal varices is not a definitive operation for portal hypertension but an emergency procedure for the immediate control of hemorrhage. A portacaval shunt of some type is required as soon after recovery from ligation as is consistent with adequate preparation for the elective procedure.

The purpose of this report is to describe an abdominal approach to ligation of esophageal varices that has proved possible in 5 consecutive cases. These patients were unselected, and the procedure was done as they were presented — some at a desirable point in their episode, and others at an unfavorable time. In all cases it was possible to perform a successful ligation of esophageal varices accompanied by cessation of bleeding. Two patients survived, and 3 died after the procedure. These cases are discussed individually below.

Technic

With the Sengstaken–Blakemore tube in place the abdomen is entered through an upper mid-line incision, and the xiphoid process removed. Median sternotomy with the use of the Lebsche osteotome could be done but has not thus far been necessary. This is the least vascular area for celiotomy, which can therefore be performed rapidly — an important consideration in patients with overdeveloped collateral venous channels in the abdominal wall. Complete exploration of the abdomen and especially of the stomach and duodenum for ulcers or other lesions can be rapidly carried out.

The terminal esophagus and stomach are exposed as in the operations of vagectomy, the repair of hiatus hernia, total gastrectomy and the Heller procedure. The left lobe of the liver is mobilized by incision of its suspensory ligament. It was feared that the large, stiff, cirrhotic liver might make the subsequent exposure of the esophagus impossible, but in all cases the lobe could be mobilized and pushed downward if not bent to the right. Case 5, in which the left lobe of the liver extended down to the umbilicus and made a tent over the spleen extending to the left wall of the chest, represented a difficult enough test of the procedure to satisfy any objection to it on this score. Figure 1 outlines the large liver, which was successfully displaced. The second step is the incision of the peritoneal reflection at the esophagogastric junction. The esophagus is easily identified. The Sengstaken–Blakemore tube should be kept inflated. By blunt-finger dissection the esophagus is encircled. A variable number of preliminary ligations of large veins at the cardioesophageal junction must be made. The next step is severance and ligation of the esophagogastric-diaphragmatic ligaments. These are identifiable bands of tissue coming off at the junction of the esophagus and stomach, whence they pass posteriorly and laterally onto the diaphragm. The esophagus is freed up in the mediastinum by blunt dissection and then pulled down into the abdomen; the inflated gastric balloon greatly facilitates this step since it can be grasped for downward traction. Further blunt dissection posterior to the esophagogastric junction is then carried out until 8 or 9 cm. of esophagus is brought down into the abdomen. When mobilization is adequate a No. 16 F. catheter is placed around the esophagogastric junction to be used for traction. The gastric balloon is then deflated. By means of a long hemostat the catheter surrounding the upper part of the stomach can be snugged up and acts as a tourniquet. This maneuver will decrease bleeding during esophagotomy since it blocks the upward flow of portal blood. The esophagus and stomach are then opened longitudinally, for about 9 cm. before the esophageal balloon is deflated. The edges are grasped with a long Babcock forceps

Figure 1. *Photograph of the Patient in Case 5, Taken after Transabdominal Ligation of Esophageal Varices, Demonstrating the Large Size of the Liver, Which Was No Deterrent to a Transabdominal Approach to the Esophagus.*

and oversewn with a running stitch if bleeding is brisk. The esophageal balloon is then deflated and withdrawn upward beyond the exposed interior of the esophagus. It is important to open a short distance into the stomach since gastric varices are often present and the bleeding area is usually at the esophagogastric junction. Varices are easily identified although the point of bleeding may not be. Usually, however, there is a reddened, swollen, berrylike area at the esophagogastric junction that looks suspicious. Ligation is begun cephalad as high as possible. A con-

tinuous locking suture of 000 chromic catgut is used, going through the mucosa, catching the veins and continuing downward over the esophagogastric junction into the stomach. Two or three groups of varices are ligated. Before the esophagus and stomach are closed the rubber catheter being used as a tourniquet to control bleeding must be released, and the interior inspected so that no bleeding point is missed. If the field is dry an ordinary sterile Levin tube is attached to the end of the Sengstaken–Blakemore tube and drawn up by the anesthetist.

Closure of the esophagus and stomach is made longitudinally by an inner continuous layer of 000 chromic catgut and a second layer of interrupted 000 silk sutures, with an occasional third layer when needed. The suture line can be reinforced by means of

FIGURE 2. *Mid-Line Incision of the Abdomen, with Xiphoid Process Resected.*

The triangular suspensory ligament of the left lobe of the liver has been severed, and the left lobe of the liver has been depressed downward and to the right, exposing the esophageal hiatus. The esophagus has been mobilized, and a tourniquet placed around the esophagogastric junction. The esophagus and stomach have been opened for 9 cm., exposing the varices within the lumen. After the varices have been oversewn (Fig. 3) the esophagus and stomach are closed longitudinally. The abdominal wall is closed in a single layer with figure-of-8 heavy-catgut sutures. No. 3 silk stay sutures are also used.

the esophagogastric-diaphragmatic ligaments, which are covered with peritoneum, or the omentum can be brought up. A Heineke–Mikulicz closure of the esophagogastric incision, which widens the junction by the technic of closing the longitudinal wound transversely, is probably not necessary since the 2 patients who survived had no serious dysphagia interfering with their alimentation. One patient experienced a short period of mild dysphagia. From a long-term point of view the Heineke–Mikulicz procedure could have disadvantages since it encourages gastric reflux and esophagitis. The abdominal wound should be closed with stay sutures. Figures 2 and 3 demonstrate the essentials of the operative technic.

Discussion

This report is presented to show that transabdominal ligation of esophageal varices is a feasible procedure. It may have wider application than the transthoracic procedure for a number of reasons previously pointed out. Chief among these is the fact that it can be used by any experienced general sur-

FIGURE 3. *Details of Suture Ligation of Esophageal Varices. Three groups of varices can be identified. The stomach must be adequately opened to ensure oversewing of the varices into the cardia and particularly over the cardio-esophageal junction.*

geon and that it provides the opportunity to deal surgically with all bleeding lesions in the upper gastrointestinal tract. Uncertainty about the site and source of bleeding has been a deterrent to early operative interference in patients with cirrhosis of the liver who bleed. As a matter of fact studies have shown that peptic ulceration occurs in a large number of patients with cirrhosis of the liver.[5,6] One of the patients in this series (Case 1) was found to have a duodenal ulcer as well as bleeding varices. A posterior gastrojejunostomy was done in addition to ligation of the varices. This abdominal procedure offers a solution to this problem, for it is probable that early surgery is the best hope for many patients with cirrhosis even though the bleeding source is a peptic ulcer. The portal hypertension present in these pa-

tients will encourage continued bleeding regardless of the source. Tamponade is useful temporarily and as a means of immediate control of bleeding from varices, but it does not seem to produce a firm clot in varices. At least, a great many of these patients bleed again.

Tamponade is a useful diagnostic test, since if it effectively stops hemorrhage, one has reasonable assurance of the site of bleeding and the source — namely varices.[7] In many patients with cirrhosis who bleed for the first time the presence of varices has never been verified. It is common practice to subject these patients to barium studies and even esophagoscopy. Sometimes, this is done immediately, and sometimes it is done after tamponade has been carried out. Often, these studies are inconclusive, and, worse still, valuable time is lost during which the patient may be losing ground. Present experience suggests that the following course of action has the most merit and offers these patients the best chance.

All patients with massive bleeding from the upper gastrointestinal tract must be carefully evaluated to disclose those with cirrhosis of the liver. The diagnostic findings are well known, and the value of liver-function tests, especially the bromsulfalein dye test, is established. If cirrhosis is present or even suspected, tamponade should be instituted. If bleeding is stopped the evidence is good that varices are the source of the hemorrhage. The patient is considered from the start a candidate for ligation of his varices, and operation delayed only long enough to prepare him for surgery by blood replacement and the correction of any fluid or electrolyte deficiency. The time needed for this is only a few hours (eight to twelve at the most). Barium studies and esophagoscopy need not be done. Neither should the patient be given a "trial" after tamponade has been discontinued to see whether or not he will bleed again. Experience at the Albany Hospital indicates that he will bleed and that his general condition rapidly deteriorates and he usually dies. Procrastination is fatal; unfortunately, it has been the order of the day in the management of these patients.

The selection of patients who have a good chance of surviving this operation and benefiting from it has not been determined. It is safe to say, however, that those whose general condition and estimated liver function would have made an elective portacaval procedure inevitable if they had not bled, are reasonable candidates. It is not known how many others who are poor risks can be salvaged by ligation of the varices. In the present series the 3 patients who died were poor risks; the 2 who survived were good candidates (Cases 1 and 5). The mortality of this and any emergency surgical procedure to correct hemorrhage will be influenced by the status of the patients who are operated upon. It has little significance when a selection of patients is made that includes only those who are fairly good risks. If early operation is performed a larger number of good-risk patients and a few poor-risk patients can be saved, and the over-all picture of bleeding from portal hypertension improved. This is not to say, however, that every patient can be subjected to this operation. Patients with evidence of very poor liver function, manifested by ascites and marked icterus, quite possibly constitute too great a risk, and often they have gone beyond the point of salvage. Hemorrhage is but a terminal event in some of these cases. Patients received for consideration late after several days of hemorrhage are also poor risks but need not be excluded. Case 2 in our series was operated upon while in coma, and after operation he became conscious with a concomitant decrease in blood ammonia; the reversal was only temporary, however. Coma is not necessarily a contraindication to surgical ligation of esophageal varices. Since it is the result of continued bleeding and ammonia intoxication, it is reasonable to believe that ligation of the varices should favorably affect coma.

Unfortunately, these patients are not always seen early by the surgeon, and a decision for or against operation must be made two, three or four days after hemorrhage has begun. Coma may be impending or present, as evidenced by high blood ammonia values or clinical findings. Coma itself need not represent a contraindication to surgery. Two of the patients in this series were in coma. This statement is made with some reservation, since a selection of patients who have a good chance of surviving ligation may be the proper confinement of operative control of bleeding. Nevertheless, it is a fact that the coma in many of these patients is the direct result of their continued bleeding, which results in an ammonia intoxication rather than further hepatic damage. One patient with a high ammonia blood level, operated upon while in coma, came out of this state after ligation (Case 2).

Post-mortem examination was performed in 2 of the 3 who died, and in neither of these was there dehiscence of the esophagogastric closure after two and eleven days.

Case Reports

Case 1. T.S., a 54-year-old man, was admitted to the Albany Veterans Administration Hospital on February 27, 1956, after having vomited an estimated 500 ml. of blood. During the previous year he had noted the onset of poor appetite, occasional nausea and vomiting associated with a weight loss of 15.9 kg. (35 pounds). Six days before admission he vomited approximately a teaspoonful of bright-red blood. This was followed 4 days later by the vomiting of 30 ml. of bright-red blood. On the day of admission he vomited approximately 1 liter of blood, part of which was red and part of which was coffee colored. There had been no previous history of jaundice, melena or previous episodes of hematemesis. He had consumed large quantities of beer for many years, in association with a very poor dietary intake.

He had enjoyed relatively good health all his life except for exertional dyspnea and angina since 1944. In June,

1952, he was admitted to the hospital for study, and the following diagnoses were made: arteriosclerotic heart disease with angina pectoris, chronic alcoholism and Laënnec's cirrhosis of the liver.

On physical examination a Grade 2 systolic murmur was audible just to the left of the sternum. The abdomen was soft and not distended. The liver was palpable, and the edge extended 11 to 12 cm. below the right costal margin. The spleen was palpable 3 cm. below the left costal margin. There was no icterus, ascites or peripheral edema.

The temperature was 99°F., and the pulse 120. The blood pressure was 110/70.

On the day of admission bromsulfalein retention was 23 per cent. The hemoglobin was 11.2 gm. per 100 ml., and the hematocrit 35 per cent. The total protein was 4.7 gm., with 2.8 gm. of albumin, and the total bilirubin 0.7 mg., the thymol turbidity 2.3 Maclagan units, the nonprotein nitrogen 32 mg., and the fasting blood sugar 82 mg. per 100 ml. The prothrombin time was 14 seconds, with a control of 13 seconds. The platelet count was 98,000, and the white-cell count 4200, with a normal differential; cephalin flocculation was + + in 24 and + + + + in 48 hours. An esophagram on the morning after admission revealed the presence of a hiatus hernia and esophageal varices. A diagnosis of cirrhosis of the liver and bleeding from esophageal varices was made.

Blood loss was replaced, the vital signs stabilized. The patient was treated conservatively. On the 9th hospital day he suddenly vomited 300 to 500 ml. of dark coffee-grounds material. The hematocrit at that time was 25 per cent, and the hemoglobin 7.6 gm. per 100 ml. A Sengstaken–Blakemore tube was passed, effectively controlling the bleeding, and studies were performed in anticipation of surgery. After transfusion the hematocrit was 38 per cent and the hemoglobin 12.4 gm., and the blood ammonia 46 microgm. per 100 ml. He was taken to the operating room on March 7, 52 hours after his 2d hemorrhage, and the upper gastrointestinal tract was explored by the transabdominal route. A chronic duodenal ulcer was found, but this was thought not to be the site of bleeding since the Sengstaken–Blakemore tube had controlled hemorrhage. An esophagotomy was then performed, and varices found. These were ligated. In addition a posterior gastrojejunostomy was carried out. During the operation, which consumed 3½ hours, the patient received 1000 ml. of whole blood and 1000 ml. of 5 per cent glucose in water. A Levin tube was left in the stomach. The procedure was tolerated well, and he was taken to the recovery room in good condition.

On the 1st day after operation his condition remained satisfactory. Blood and electrolyte studies were within normal limits. On the 2d day a right-lower-lobe pneumonitis developed, rapidly responding to antibiotic therapy. At no time in the postoperative period was there any evidence of bleeding from the upper gastrointestinal tract. The patient was given a period of medical therapy that resulted in marked improvement in his liver function after 1 month, as manifested by a drop in retention of bromsulfalein from 23 to 3 per cent at the end of 45 minutes. The total value for protein rose to 6.5 gm. per 100 ml., with 3.6 gm. of albumin. He underwent a portacaval shunt on May 10, approximately 2 months after emergency ligation of esophageal varices.

Case 2. C.C., a 45-year-old man, was admitted to the Albany Hospital on March 1, 1956, by transfer from another hospital for the treatment of bleeding associated with liver cirrhosis. He had had 2 admissions in the past for bleeding varices, the 1st episode occurring 2 years previously and the 2d lasting from January 12 to January 24, 1956. On February 29, he was admitted to the Kingston Hospital, having been vomiting coffee-grounds material for 1 day. He also seemed to be becoming progressively comatose. After 8 hours he was transferred to the Albany Hospital.

He had never been seriously ill except for the disease described in the present illness. He admitted to drinking 1 quart of whisky a day for 8 years.

Physical examination showed a pale, dry and lethargic man. During the examination he continued to vomit dark material. There were numerous spider angiomas over the chest, and the liver and spleen were palpably enlarged. No evidence of jaundice or venous collateral was seen. He was disoriented and hyporeflexic, and a flapping tremor of the upper extremities was noted.

The blood pressure was 146/78, the pulse was 130.

The hematocrit was 29 per cent, and the plasma was icteric. The glucose was 183 mg., and the nonprotein nitrogen 23 mg. per 100 ml. The prothrombin time was 30 per cent of normal. The total protein was 5.9 gm., with an albumin of 2.5 gm., and the total bilirubin 2.0 mg. per 100 ml. The serum sodium was 130 milliequiv., the potassium 2.7 milliequiv., the chloride 105 milliequiv., and the carbon dioxide combining power 20 milliequiv. per liter. The blood ammonia nitrogen was 91 microgm. per 100 ml. Urinalysis revealed a + + + test for sugar, a + + test for diacetic acid and a + + test for bile.

A Sengstaken–Blakemore tube was passed, and the stomach aspirated. Supportive therapy was instituted, and within 2 hours the patient was awake and rational, and the vital signs were stable. On the following morning he was again stuporous, and the hemoglobin was 9 gm. per 100 ml., and the hematocrit 26 per cent. He received additional blood and again improved. Neurologic examination revealed the presence of bilateral Babinski reflexes. The tube was deflated on the 3d hospital day and removed on the 4th. The patient did quite well; he was awake and in contact with his environment. Because the hematocrit value was 30 per cent another 500 ml. of blood was given. On the 5th hospital day thrombophlebitis at the site of an intravenous catheter developed. On the following day he was noted to have a right-lower-lobe pneumonitis and once again became lethargic, with slurred speech. The blood ammonia nitrogen was 141 microgm., and the pyruvic acid 1.35 mg. per 100 ml. That evening he vomited bright-red blood, passed tarry stools and lapsed into a coma. The Sengstaken–Blakemore tube was once again passed, the stomach evacuated, and replacement transfusions given. On the 7th hospital day the blood ammonia was 150 microgm., and the pyruvic acid 1.90 mg. per 100 ml. Sodium glutamate and thioctic acid were administered. It was decided that the esophageal varices should be ligated although the patient's status was not good. Preoperatively, the blood ammonia nitrogen was 266 microgm., and the pyruvic acid 2.35 mg. per 100 ml. He was in coma, and ligation of his varices was undertaken in a desperate situation after a long period of bleeding (8 days).

Through a transabdominal approach the varices were ligated, and liver biopsy performed. The entire procedure took 3 hours and 20 minutes, during which he received 2000 ml. of whole blood. Blood loss was estimated at 2100 ml. On the following day he remained incoherent and lethargic. The hematocrit was 34 per cent, and the blood ammonia nitrogen 111 microgm., and the pyruvic acid 2.20 mg. per 100 ml. On the 2d postoperative day he was awake and co-operative; the blood ammonia nitrogen had fallen to 92 microgm. per 100 ml. He did well until the evening of the 4th postoperative day, when he again became disoriented and the temperature rose to 103°F. (this was attributed to a bilateral bronchopneumonic process). He improved on antibiotics and supportive therapy until the 8th day, when he began to have gasping respiration, an icteric tint to the skin and incoherent speech. The blood ammonia values did not become elevated, however (54 and 82 microgm. per 100 ml.). He died on the 8th postoperative day.

At no time in the postoperative period was there any evidence of recurrence of the bleeding from the varices. The indwelling Levin tube returned clear intestinal fluid. Postmortem examination revealed an acute bilateral bronchopneumonia. There had been no leak from the esophageal wound. The diagnosis of cirrhosis of the liver and esophageal varices was confirmed. This patient was operated upon late after a 2d bleeding episode that followed a primary one controlled temporarily by the Sengstaken–Blakemore tube. It was believed in retrospect that his best chance would have been to have undergone ligation at the time of admission.

Case 3. A.H., a 68-year-old man, was admitted to the Albany Veterans Administration Hospital on March 13, 1956, having been transferred from another hospital because

of tremor and a semistuporous level of consciousness. He had had a history of liver disease dating back to at least 1951, when he noted the onset of progressive enlargement of the abdomen associated with ascites. From 1951 to 1953 this ascites was adequately controlled by biweekly injections of mercurial diuretics. In 1953 he became refractory to this regimen and was admitted to a hospital for study. After this, the ascites became better controlled on a regimen of high-protein, low-salt diet in conjunction with diuretics. Two days before the present admission he voluntarily stopped all fluid intake and shortly thereafter became stuporous. He denied excessive or even moderate use of alcohol. This was confirmed by his family.

No serious diseases were reported except as noted in the present illness.

Physical examination showed a man weighing 79.8 kg. (176 pounds). Positive findings included large areas of vitiligo and pigmentations over the body, a Grade 3 precordial murmur transmitted to the neck and a greatly distended abdomen with fluid wave and shifting dullness demonstrable. A small umbilical hernia and a markedly enlarged, easily ballotable spleen were found. The liver was not palpably enlarged.

The temperature was 98°F., and the pulse 80. The blood pressure was 170/90.

Examination of the blood disclosed a hemoglobin of 10.9 gm. per 100 ml., with a hematocrit of 34 per cent, and a white-cell count of 6400, with a normal differential. The following chemical examinations were obtained: serum bilirubin, 2.5 mg. per 100 ml.; thymol turbidity, 8.1 units; prothrombin time, 19 seconds (control, 12 seconds); total protein 5.4 gm. per 100 ml., with an albumin of 2.6 gm.; and cephalin flocculation ++++. There was 31 per cent retention of bromsulfalein at the end of 45 minutes. The fasting blood sugar was 100 mg., and the nonprotein nitrogen 58 mg. per 100 ml. The values for serum sodium, potassium chloride and carbon dioxide combining power were within normal limits. The blood ammonia nitrogen was 61 microgm. per 100 ml.

During the 1st week in the hospital the patient remained asymptomatic on sodium restriction and diuretic therapy, but on the 6th hospital day he vomited approximately 1000 ml. of bright-red blood and a mild degree of hypotension developed. The Sengstaken–Blakemore tube was passed, and replacement transfusions given. The tube was deflated at the end of 24 hours and removed at the end of 48 hours. Because of the patient's age and cardiovascular status operative ligation was not undertaken at this time. On the following day he again vomited 1000 ml. of bright-red blood. The tube was reinserted and it was decided to ligate the bleeding varices through a transabdominal approach. The blood ammonia had risen to 561 microgm. per 100 ml. During the operative procedure the esophagus was ruptured inadvertently by sudden overdistention of the esophageal balloon, the rent extending upward to the aortic arch. The abdominal incision was extended into the chest, and the defect closed. During the entire procedure, which took 3½ hours, the estimated blood loss was 2000 ml. He received 2000 ml. of whole blood and 1000 ml. of 5 per cent glucose in water.

He did well in the immediate postoperative period, but shortly thereafter the blood pressure began to fall. The hemoglobin was 10.9 gm. per 100 ml., and the hematocrit 35 per cent. A roentgenogram of the chest taken with a portable machine revealed the presence of a moderate hemopneumothorax. His condition rapidly deteriorated despite intravenous administration of Eschatin, Cortef and Levophed. He died in the recovery room 16 hours after operation. He had received a total of 7.5 liters of blood during his hospital stay. At post-mortem examination no evidence of suture leak or abnormal bleeding was found to account for the terminal state of shock. The diagnosis of cirrhosis of the liver and esophageal varices was confirmed. About 400 ml. of old blood was present at the operative site. The patient had become considerably jaundiced and evidenced marked liver failure.

Again, operative ligation of esophageal varices was undertaken late and should have been done at the time of the 1st bleeding episode.

Case 4. P.S., a 58-year-old widowed man was admitted to the Albany Hospital via the emergency room on March 14, 1956, because of intermittent vomiting of blood of 12 hours' duration. For an unspecified time he admitted to the ingestion of 2 quarts of beer daily, but relatives reported constant use of large quantities of beer, whisky and, more recently, wine and radiator antifreeze. Two years before admission he noticed the onset of symmetrical enlargement of the abdomen and, more recently, the onset of flatulence. On the day of admission he experienced 8 episodes of hematemesis over a 12-hour period associated with the passage of bright-red blood by rectum. There was no previous history of hematemesis, melena or jaundice.

He had been in fairly good health except for a comminuted fracture of the left femur sustained in September, 1951.

Physical examination disclosed a pale, well developed, well nourished, acutely ill man. The positive findings included a rapid heart rate with occasional premature ventricular contractions, a symmetrically distended abdomen, with shifting dullness in the flanks, an enlarged, firm, coarsely irregular liver, palpable 10 cm. below the right costal margin, and the presence of ulcerations and pigmentation over both anterior tibial regions. No angiomas, liver palms, splenomegaly or hemorrhoids were demonstrated.

The temperature was 98°F., and the pulse 100. The blood pressure was 80/50.

The hematocrit was 29 per cent. The nonprotein nitrogen was 36 mg., and the total proteins 6.4 gm. per 100 ml., with 3.0 gm. of albumin. The total bilirubin was 9.3 mg., and the thymol turbidity 7.8 Maclagan units per 100 ml., and the prothrombin time 17 per cent of normal. The serum sodium was 131 milliequiv., the potassium 3.9 milliequiv., the chloride 93 milliequiv., and the carbon dioxide combining power 23 milliequiv. per liter. The blood ammonia nitrogen was 106 microgm. per 100 ml.

The esophageal bleeding was controlled by balloon tamponade. The patient received 2000 ml. of whole blood, 250 ml. of pooled plasma and 1000 ml. of glucose in water, with added vitamin K, before the blood pressure and pulse stabilized. Castor oil was immediately given via the tube to rid the bowel of ammonia-producing blood products. Blood studies on the following day revealed the ammonia to be 75 microgm., and the pyruvic acid 2.90 mg. per 100 ml. He was maintained with supportive measures, including daily use of blood and plasma, limited sodium intake, vitamin K and 10 per cent glucose in water. On March 17, 72 hours after admission, bleeding recurred because of loosening of the tube. Owing to persistent bleeding it was considered worth while to attempt ligation of the varices. On March 18 a transabdominal ligation was performed during which an estimated 1600 ml. of blood was lost; 1500 ml. of whole blood was given during the procedure, which lasted for 3 hours. He was removed in good condition to the Special Nursing Unit for further care.

On the day after operation the blood ammonia was 378 microgm., and the pyruvic acid 3.3 mg. per 100 ml. The hematocrit was 33 per cent, and the potassium 3.3 milliequiv., the sodium 123 milliequiv., the carbon dioxide combining power 23 milliequiv., and the chloride 90 milliequiv. per liter. Because of the elevated blood pyruvate, thioctic acid was administered. On the following day the patient became increasingly stuporous, urinary output diminished greatly, and the temperature was elevated to 103°F. The blood ammonia at this time was 528 microgm., and the pyruvic acid 5.45 mg. per 100 ml. Thioctic acid, Eschatin and hydrocortisone were given, but the vital signs progressively deteriorated, and he died on the 2d postoperative day.

During his hospital stay he received a total of 7 liters of blood. At no time was there evidence of recurrence of bleeding from the varices after ligation. Liver function was extremely poor, and ligation was done in an attempt to salvage a patient who was a very poor risk. Earlier operative ligation should have been considered. Death was due to progressive liver failure. Post-mortem examination was not performed.

Case 5. J.M., a 47-year-old man, was admitted to the Albany Veterans Administration Hospital on March 26, 1956, because of the vomiting of blood. He had been discharged from the Army in 1943 after he was found to have cirrhosis of the liver. Previously, he had at least a 10-year history of sparse dietary intake in association with the in-

gestion of up to 30 glasses of beer daily. Except for occasional right-upper-quadrant pain he had remained well since discharge until 1 day before admission, when he had 3 episodes of massive hematemesis. On the day of admission he noticed the passage of tarry stools. There was no history of ascites, jaundice, edema or previous bleeding.

He had been in fair health most of his life. No serious illnesses, operations or accidents were revealed in the past history.

Physical examination showed a thin man who appeared chronically ill. The positive findings included pallor of the skin, a Grade 1 apical systolic murmur and a hard, nodular liver enlarged to the level of the umbilicus and palpable in the left upper quadrant as well. There was no evidence of angiomas, icterus, ascites or peripheral edema.

The temperature was 98°F., and the pulse 110. The blood pressure was 120/70.

Examination of the blood disclosed a hemoglobin of 7.6 gm. per 100 ml., a hematocrit of 24 per cent and a white-cell count of 13,500. The nonprotein nitrogen was 50 mg. per 100 ml., the prothrombin time 17 seconds (control, 13 seconds), and the serum sodium 138 milliequiv., and the potassium 4.7 milliequiv. per liter. The bilirubin was 2.1 mg., and the thymol turbidity 6.6 Maclagan units per 100 ml. The total protein was 5.8 gm. per 100 ml., with 4.2 gm. of albumin. Urinalysis showed a + reaction for albumin and a + + + + test for sugar.

The esophageal bleeding was controlled by introduction of the Sengstaken–Blakemore tube, and replacement transfusions and supportive therapy were given to prepare the patient for surgery, which was decided upon at once. After stabilization of the vital signs transabdominal ligation of the bleeding varices was performed 8 hours after admission. An indwelling Levin tube was left in place. During the 2½-hour operation the estimated blood loss was 1400 ml. While in the operating room he received 1300 ml. of whole blood and 500 ml. of 5 per cent glucose in water.

He withstood the procedure well and was taken to the recovery room in good condition. On the 1st postoperative day his condition remained satisfactory except for a slight elevation of temperature. The blood pressure was stable. The hemoglobin was 11.5 gm., the serum bilirubin 2.1 mg., and the blood ammonia 149 microgm. per 100 ml. Electrolytes were within normal range. Medications consisted of penicillin, streptomycin, vitamins, with additional vitamin K, intravenous infusions of fluids and sufficient milk of magnesia to remove any accumulated blood from the gastrointestinal tract. Three days after operation the patient became mentally confused and disoriented. The blood ammonia at this time was found to be 307 microgm. per 100 ml.; administration of 100 ml. of 20 per cent glutamic acid solution gradually reduced this to a normal level. At no time in the postoperative period was there evidence of renewed bleeding. After this convalescence was uncomplicated except for intermittent crampy abdominal pain somewhat suggestive of a partial small-bowel obstruction. Six weeks after admission he was being prepared for portacaval shunt. Figure 1 is a photograph of this patient's abdomen, outlining the liver. The large size of this liver, especially the left lobe, was not a deterrent to transabdominal ligation of varices.

Summary and Conclusions

A technic for the ligation of bleeding esophageal varices in patients with portal hypertension by means of the abdominal route is described. This procedure was performed in 5 consecutively observed patients with cirrhosis of the liver and a bleeding episode. These patients were operated on at different stages in their episodes. In all cases bleeding was successfully controlled, as evidenced by gastric aspiration and the clinical course in the postoperative period and by post-mortem examination on the patients who died. Three patients did not survive. The patients were poor risks from the standpoint of the status of their liver disease and the lateness of their surgery.

The question of whether or not surgical ligation of varices is justified in poor-risk patients with liver disease is not established. There is convincing evidence, however, that the method of esophagogastric tamponade is inadequate and temporary, and that control of hemorrhage by surgical ligation is the only certain method. It also seems clear that patients whose liver function is fairly good are favorable candidates for ligation. The earlier operation is decided upon and undertaken, the better the chance of survival.

The transabdominal route offers a solution to diagnostic problems concerned with the determination of the bleeding source since both esophageal varices and ulcerating lesions of the stomach can be dealt with.

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NEEDLE BIOPSY OF THE PARIETAL PLEURA*

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CHICAGO

CLINICAL analysis and the application of traditional laboratory methods[1] usually enable a clinician to determine the cause of an "idiopathic pleural effusion," but considerable time may elapse before a diagnosis is definitely established. It has become a matter of good practice initially to consider such an effusion in a young person as a manifestation of tuberculosis, and in older patients as a sign of pleural involvement by neoplastic disease, and then to defer definite diagnosis until further observation has confirmed or invalidated these initial impressions. As far as tuberculosis is concerned, this practice appears to be justified by the fact that idiopathic pleural effusion is often followed by clinically evident pulmonary tuberculosis within months or years.[2-4] The frequent failure to demonstrate the tubercle bacillus in the aspirated fluid has been explained by the important role of hypersensitivity in the pathogenesis of tuberculous pleural effusion.[4,5] A small subpleural tuberculous lesion may lead to infection of the pleura and, in the presence of hypersensitivity, to an extensive inflammatory exudation.[4,5] The resulting marked dilution of tubercle bacilli may prevent their detection by the usual means of smear, culture and guinea-pig inoculation.

FIGURE 1. *Surgical Biopsy of the Pleura in Patient T. B., Showing Granulomatous Inflammation (X94). Note the layer of palisading cells.*

The pathological changes of caseation and tubercle formation in tuberculosis of the pleura have been extensively studied at autopsy,[6,7] but observations of the diseased pleura during life were rare before the discovery of antituberculous chemotherapeutic agents and the development of more radical surgical technics.

In 1925 Jacobaeus[8] reported on thoracoscopic observations in patients with pleural tuberculosis. He found the pleura studded with tubercles. This observation was incidental to the use of thoracoscopy for the separation of adhesions impeding the effectiveness of a therapeutic pneumothorax, and did not lead to the utilization of thoracoscopy as a diagnostic technic in patients with idiopathic pleural effusion until recently. The performance of even minor thoracic surgical procedures in patients suspected of having acute tuberculosis was considered too hazardous before the discovery of effective antituberculous drugs. In patients with suspected malignant invasion of the pleura, Lloyd[9] recently recommended pleural biopsy under thoracoscopic observation, and performed this procedure in 23 such patients; in 12. the biopsy revealed malignant neoplasm.

Direct biopsy of the pleura during thoracotomy has been performed by several investigators during recent years. Stead, Eichenholz and Stauss[10] could demonstrate tuberculosis in the tissue removed during decortication in only 15 out of 24 patients suspected of having tuberculous pleural effusions. The results of this study emphasize the frequency of pleural effusions that are apparently nontuberculous. Sutliff, Hughes and Rice[11] studied 21 patients by using the method of a small thoracotomy, and demonstrated tuberculosis in 17 patients, carcinoma in 2 and blastomycosis in 1. Small and Landman[12] found pleural tuberculosis in biopsy specimens obtained during thoracotomy in 5 patients who were subjected to this procedure because of an uncertain clinical diagnosis.

Our experience with pleural biopsy, obtained by Klassen's[13] technic of small thoracotomy, is limited to a few patients in whom it was of great diagnostic help.¶ In some it revealed unusual and unexpected disease, as in the following case:

T.B., a 56-year-old man, who had suffered from rheumatoid arthritis for 2 months, manifested a pleural effusion and a small infiltrate in the right upper lobe. Cultures of the pleural fluid remained negative. Cell-block examination revealed giant cells. The impression, therefore, was tuberculous pleural effusion. Surgical biopsy of the pleura by

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Presented at the Fifteenth Veterans Administration — Army-Navy Conference on the Chemotherapy of Tuberculosis, St. Louis, Missouri, February 6-9, 1956.

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¶We are indebted to Dr. Melvin I. Gibbel, chief, Surgical Service, and to Dr. John L. Keely, attending surgeon in thoracic surgery, West Side Veterans Administration Hospital, Chicago, for permitting us to refer to these surgical biopsies, which were performed on their service.

Klassen's[13] technic disclosed inflammatory changes characterized by the palisading of histiocytes underneath a layer of fibrinoid degeneration. These findings were interpreted as rheumatoid pleuritis (Fig. 1).

Biopsy by this technic also facilitated and accelerated the diagnosis of tuberculosis in 2 patients, and helped to exclude tuberculosis in 2 others.

This method, therefore, can be considered of great value. It has several disadvantages: it is a surgical procedure that has to be performed in an operating room by a skilled thoracic surgeon; it requires anesthesia and often tracheal intubation; and it may result in postoperative morbidity. Thus, it seems unlikely that surgical biopsy of the pleura will attain the degree of widespread use that is necessary for the differential diagnosis of a disease as common as pleural effusion.

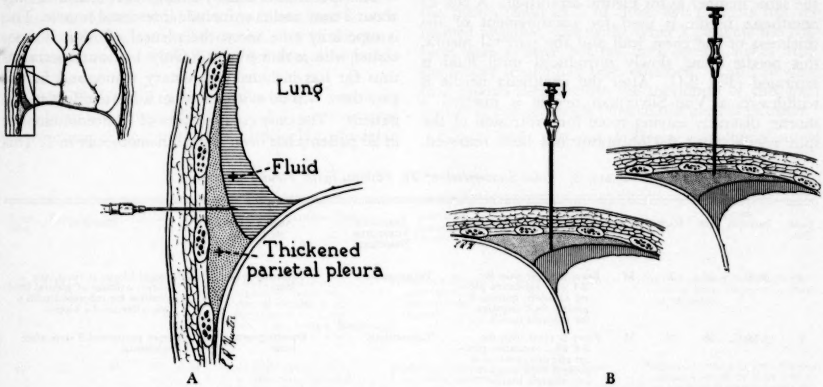

FIGURE 2. *Procedure for Needle Biopsy of the Parietal Pleura, Showing the Anesthesia Needle in the Pleural Space* (A) *and the Position of the Vim–Silverman Needle before and after Advancement of the Split Needle* (B).

TABLE 1. *Needle Biopsy of the Parietal Pleura (20 Patients).*

DIAGNOSIS	NO. OF CASES
Caseating granuloma	5
Neoplasm	4
Fibrosis	9
Insufficient specimen	2

During the past three years we have occasionally performed biopsy of the parietal pleura with the Vim–Silverman needle in older patients with suspected carcinoma. Only since 1954, however, has this technic been applied to a systematic study of all patients with pleural effusion in whom the etiologic diagnosis could not be readily established by traditional means. Encouraged by the early results and the lack of morbidity, we have frequently performed this procedure in patients early in their disease, before the report on the cultures or cell block was obtained.

Independently, this technic has also been used in 6 patients with pleural effusion by DeFrancis, Klosk and Albano,[14] and evidence of tuberculous pleuritis has been obtained in 2 of these patients. Also, Katz, Donohoe and Mathews[15] found this simple technic useful in the differential diagnosis of pleural effusion.

TABLE 2. *Biopsy and Clinical Diagnosis in 18 Patients with "Idiopathic" Pleural Effusion.*

BIOPSY DIAGNOSIS	NO. OF CASES	INITIAL CLINICAL DIAGNOSIS	NO. OF CASES	FINAL DIAGNOSIS	NO. OF CASES
Caseating granuloma	5	Tuberculosis	3		
		Neoplasm	2	Tuberculosis	5
Neoplasm	4	Neoplasm	4	Neoplasm	4
Nonspecific fibrosis	9	Tuberculosis	5	Bronchogenic carcinoma (autopsy)	1
		Neoplasm	5	Congestive heart failure (autopsy)	1
				Obstruction of lymph channels by lymphoma (autopsy)	3
				Post-traumatic pleuritis	1
				Pulmonary infarct	1
				Postpneumonic pleural effusion	2

Procedure

Needle biopsy of the pleura is easily performed. After it has been ascertained that the patient has no coagulation defect, the site of the biopsy is selected fluoroscopically. The patient's skin is prepared in the same manner as for pleural aspiration. A No. 22 anesthesia needle is used for measurement of the thickness of the chest wall and the parietal pleura, this needle being slowly introduced until fluid is aspirated (Fig. 2*A*). After the anesthesia needle is withdrawn a Vim–Silverman needle is inserted a shorter distance, leaving room for protrusion of the split needle after the obturator has been removed. The split needle is advanced (Fig. 2*B*) and rapidly rotated in a manner similar to the technic of liver biopsy, and then the entire unit is speedily withdrawn. If pleural fluid cannot be aspirated, but resistance to the anesthesia needle indicates marked thickness of the pleura, a biopsy can still be performed. We have not attempted pleural biopsy when an obliterated costophrenic angle was the only evidence of pleural disease.

The specimen is usually small, often measures only about 3 mm. and may include intercostal muscle. This is especially true when the pleural effusion is associated with a thin pleura. Only 1 of our specimens thus far has included pulmonary tissue, and in this case there was no evidence of an adverse effect to the patient. The only complication of 22 needle biopsies in 20 patients has been a small hemothorax in 1. This was recognized by an increase of the pleural effusion after biopsy and did not cause any serious consequence to the patient. A chest roentgenogram should be obtained twenty-four hours after biopsy.

Table 3. *Case Summaries of 18 Patients with Pleural Disease.*

Case No.	Initials	Age	Race	Sex	Pertinent Clinical Data	Initially Suspected Diagnosis	Needle Biopsy of Pleura	Remarks
		yr.						
1	M.P.	33	N	M	Fever & chest pain for 3-4 wk.; exudative pleural effusion; sputum & pleural fluid negative for tubercle bacilli.	Tuberculosis	Caseating granuloma	Surgical biopsy showed only fibrin; cultures of pleural fluid positive for tubercle bacilli 6 wk. after needle biopsy.
2	J.McK.	38	N	M	Fever & chest pain for 3-4 wk.; exudative pleural effusion; sputum & pleural fluid negative for tubercle bacilli.	Tuberculosis	Caseating granuloma	Biopsy performed 3 days after admission
3	B.B.	34	N	M	Enlarged cervical lymph nodes since April, 1954; biopsy diagnosis, lymphosarcoma; April, 1955, infiltration of rt. lower lobe & rt.-sided pleural effusion.	Lymphosarcoma of lung & pleura; pulmonary infarct?	Caseating granuloma	Sputum & cultures of pleural fluid positive for tubercle bacilli 6 wk. after biopsy; death due to gastrointestinal hemorrhage.
4	F.P.	64	W	M	Weight loss, chest pain & unproductive cough of 3 wk. duration; lt.-sided pleural effusion.	Metastatic carcinoma of pleura	Caseating granuloma	Excellent response to antituberculous therapy
5	J.S.	38	N	M	Weight loss, mild fever & gradually increasing swelling of abdomen; chronic alcoholism; small pleural effusion on rt.; ascites.	Disseminated tuberculosis; cirrhosis of liver.	Caseating granuloma	Laparotomy revealed peritoneal tuberculosis; excellent response to antituberculous therapy.
6	F.M.	68	W	M	Weight loss & chest pain; several thoracenteses; no diagnostic studies before admission.	Metastatic carcinoma	Anaplastic carcinoma	Biopsy diagnosis obtained 48 hr. after admission; cell block showed suspicious cells.
7	W.S.	67	W	M	Weight loss & vague chest pain of 6 wk. duration; rt.-sided pleural effusion.	Metastatic carcinoma	Mesothelioma	Cell block showed atypical cells; autopsy confirmed diagnosis of mesothelioma.
8	D.B.	34	W	M	Hodgkin's disease of 1 yr. duration; pleural effusion for few days before admission; pleural-fluid transudate.	Lymphoma?; radiation fibrosis?	Hodgkin's sarcoma invading chest wall	No abnormal cells seen in cell block
9	J.U.	60	W	M	Chest pain & weight loss for 3 mo. before admission	Metastatic carcinoma	Adenocarcinoma	Cell block showed malignant cells; primary site unknown; no autopsy.
10	P.R.	44	N	M	Chest pain of several wk. duration; pleural effusion; paralysis of rt. leaf of diaphragm.	Bronchogenic carcinoma	Nonspecific fibrosis, with foci of necrosis	Cell block showed malignant cells; needle biopsy failed to establish diagnosis.
11	J.M.	30	W	M	Rheumatic fever in childhood; mitral stenosis & aortic insufficiency; several episodes of congestive heart failure in past; pleural effusion, which persisted for 1 yr. despite control of congestive heart failure.	Tuberculosis?; disseminated lupus erythematosus?; pulmonary infarction?; rheumatic pleuritis?	Nonspecific fibrosis	Patient died of paroxysmal ventricular tachycardia; autopsy showed nonspecific pleural fibrosis.

Results

The histologic diagnoses of the biopsy specimens fall into four groups (Table 1). A caseating granuloma was found in 5 cases. This designation was preferred to the term tuberculous granuloma, since the specimens were not used for bacteriologic study. Neoplasm was demonstrated in 4 specimens, and a nonspecific type of pleural fibrosis was seen in 9 others. Two specimens were insufficient for adequate pathological study.

Analysis of the 5 patients in whom a caseating granuloma was found (Tables 2 and 3) demonstrates the common clinical problem with which a physician is often faced when he has only the traditional methods of examination available. The diagnosis of tuberculosis was suspected in only 3 of these patients (Cases 1, 2 and 5 of Table 3) before biopsy, and neoplastic disease appeared to be more likely in the other 2 since 1 (Case 3) had a lymphosarcoma of the cervical lymph nodes, and the other (Case 4) was sixty-four years old. The tuberculin test was positive in all 5 patients whereas the histoplasmin, coccidioidin and the blastomycin tests were negative. Culture of the pleural fluid in 3 of these five patients has remained negative, and in the other 2 patients the cultures were positive but not until several weeks after the biopsy results had been obtained. The following case reports demonstrate the usefulness of this procedure in patients with tuberculous pleural effusion:

Case 1. M.P., a 33-year-old Negro, was admitted to the hospital with an idiopathic pleural effusion (with the characteristics of an exudate), and was considered to have tuberculosis, in spite of numerous negative cultures of the sputum, pleural fluid, gastric content and bronchoscopic aspirate. After he had undergone an unsuccessful pleural biopsy dur-

Table 3. *(Concluded).*

Case No.	Initials	Age	Race	Sex	Pertinent Clinical Data	Initially Suspected Diagnosis	Needle Biopsy of Pleura	Remarks
		yr.						
12	D.G.	66	W	M	Hodgkin's disease of several yr. duration; pleural effusion & infiltration in rt. lower lobe 3 mo. before death; x-ray therapy to chest.	Hodgkin's disease?; tuberculosis?; postradiation fibrosis?	Nonspecific fibrosis	Autopsy showed Hodgkin's disease of lung; nonspecific fibrosis of pleura.
13	J.S.	61	N	M	Hodgkin's disease of 5 yr. duration; bilateral pleural effusion of several wk. duration.	Hodgkin's disease involving pleura	Nonspecific fibrosis	Patient has had bilateral chylous effusion for more than 1 yr.; is working & requires only occasional thoracentesis.
14	R.P.	64	W	M	Chronic lymphatic leukemia for 2 yr., treated with triethylene melamine; patient lost weight & pleural effusion & hemolytic anemia developed 4 wk. before admission; pleural fluid contained lymphocytes & had low protein content and low specific gravity.	Tuberculosis?; lymphoma?	Nonspecific fibrosis	Pleural effusion disappeared after steroid therapy; no relapse during observation period of 3 mo.
15	E.R.	59	W	M	Progressive shortness of breath of about 2 yr. duration; pulmonary emphysema; development of increasing reticulation of lung; pleural effusion.	Disseminated tuberculosis?; metastatic carcinoma?	Nonspecific fibrosis	Patient responded well to steroid therapy & much improved 7 mo. after onset of severe dyspnea; pleural effusion disappeared; clinical diagnosis still uncertain, but fulminant pulmonary fibrosis being considered.
16	A.L.	37	W	M	Morphine addict; chest pain, weight loss & fever of 1 mo. duration; rt.-sided hemorrhagic pleural effusion.	Tuberculosis?; pulmonary infarct?	Nonspecific fibrosis	Pleural effusion subsided spontaneously; most likely diagnosis, pulmonary infarct.
17	J.F.	27	W	M	Recurrent pleuritic pain bilaterally since automobile accident 5 mo. before admission; small bilateral pleural effusion; past history of several bouts of pneumonia; only thick pleura found on attempts at aspiration.	Hemothorax due to trauma?; tuberculosis?	Nonspecific fibrosis	Patient probably had bilateral small hemothorax after automobile accident (steering-wheel injury)
18	J.N.	66	W	M	Pulmonary tuberculosis 1919-1924; cough & weight loss for 6 mo. after pneumonia; hemorrhagic pleural effusion.	Bronchogenic carcinoma	Pleural fibrosis	Pleural effusion disappeared; patient well during observation period of 6 mo.

ing small open thoracotomy, a needle biopsy of the pleura was performed, demonstrating a caseating granuloma. Six weeks later a 6th pleural-fluid culture was reported positive for tuberculosis.

CASE 2. J.Mc., a 38-year-old Negro construction worker, was admitted to the hospital with symptoms of chest pain, malaise, weight loss and mild fever of 3 weeks' duration. A pleural exudate was found, and 7 pleural-fluid cultures were negative. Needle biopsy of the pleura 3 days after admission showed a caseating granuloma. A tuberculin test was positive; coccidioidin, histoplasmin and blastomycin skin tests were negative.

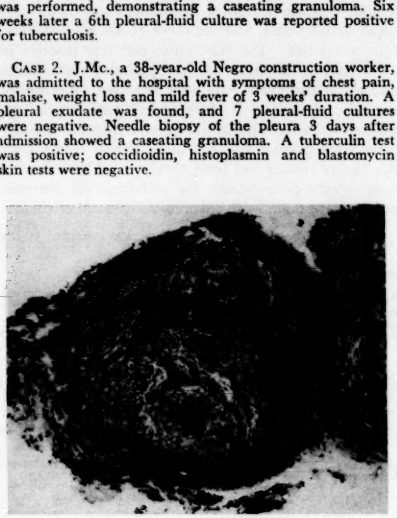

FIGURE 3. *Needle Biopsy of the Pleura in Case 4 (Table 3), Showing Caseating Granuloma (X94).*

CASE 3. B.B., a 34-year-old Negro with lymphosarcoma of the cervical lymph nodes, had a pleural effusion that was assumed to be due to lymphosarcoma. Pleural biopsy revealed an inflammatory lesion with small areas of necrosis and a giant cell. Six weeks later cultures of the pleural fluid were positive, and several months later autopsy revealed the presence of both lymphosarcoma and tuberculosis.

CASE 4. F.P., a 64-year-old man, was admitted to the hospital with a pleural effusion of recent onset. This was considered to be due to neoplastic disease, but needle biopsy of the pleura demonstrated a granuloma with caseation (Fig. 3).

Four patients were found to have neoplastic disease involving the pleura. In each of these cases the initial clinical impression was neoplastic disease causing pleural effusion, but examination of the cell block gave only inconclusive results. A tissue diagnosis was obtained by means of a pleural biopsy within a few days of admission; there was no more discomfort to the patient than a pleural aspiration would have caused. The following reports serve to illustrate the helpful information obtained by pleural biopsy in these cases.

CASE 6. F.M., a 68-year-old man, had recurrent pleural effusion for about 1 year before admission. This was treated with repeated pleural aspirations, but a definite diagnosis was not made. A pleural biopsy 2 days after admission revealed anaplastic carcinoma (Fig. 4). The aspirated fluid showed only suspicious cells on cell-block examination. Autopsy 6 weeks later confirmed the diagnosis of malignant invasion of the pleura.

CASE 7. W.S., a 67-year-old man, was admitted to the hospital with vague pain in the right side of the chest of 6 weeks' duration. A right-sided pleural effusion with the characteristics of an exudate was found, and atypical cells were seen on cell block. Needle biopsy of the pleura revealed a malignant mesothelioma (Fig. 5). This was confirmed several months later at autopsy.

CASE 8. D.B., a 34-year-old man, who had been known to have Hodgkin's disease for 1 year, was admitted to the hospital because of dyspnea of recent onset. A large left-sided pleural effusion was present, and the aspirated fluid had the characteristics of a transudate. No abnormal cells were seen in the sections of the cell block, and it was the clinical impression that the pleural effusion was secondary to postirradiation fibrosis. A pleural biopsy showed that Hodgkin's sarcoma had developed and had invaded the chest wall. This was confirmed several weeks later at autopsy.

In addition to these 4 patients, there were 2 with carcinoma and pleural effusion in whom this procedure did not give helpful information. One (Case 10, Table 3) had a bronchogenic carcinoma, proved by bronchoscopy and cell block from the pleural fluid; at autopsy malignant infiltration of the pleura that had caused a marked desmoplastic reaction was demonstrated. The other patient also had broncho-

FIGURE 4. *Needle Biopsy of the Pleura in Case 6 (Table 3), Showing Anaplastic Carcinoma (X94).*

genic carcinoma with a small pleural effusion; the specimen obtained on pleural biopsy was unsatisfactory for tissue examination. A thoracotomy revealed an inoperable carcinoma, but no pleural infiltration could be demonstrated. Autopsy several weeks later revealed bronchogenic carcinoma and metastatic involvement of one rib, with local extension into the pleura over an area of about 3 cm. There was no pleural effusion, and no other pleural involvement was found.

The 9 patients in whom pleural biopsy disclosed only nonspecific pleural fibrosis require special attention in this analysis because of the obvious possibility that the small piece of tissue in the Vim–Silverman needle is not a representative sample of the diseased pleura. As previously mentioned, the pleural fluid of 1 patient (Case 10, Table 3) contained malignant cells whereas the pleural biopsy disclosed only non-

specific pleural fibrosis. In this case the needle biopsy failed to disclose the diagnosis, which was established by other means. This failure can probably be explained by the patchy distribution of the pleural metastases and the marked pleural fibrosis that were found at autopsy. It is possible that repetition of the biopsy at a different area would have resulted in the correct diagnosis, but in view of the presence of malignant cells in the cell block this was not done.

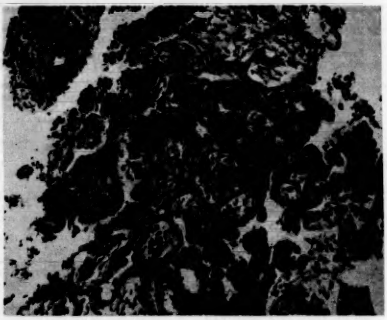

FIGURE 5. *Needle Biopsy of the Pleura in Case 7 (Table 3), Showing Mesothelioma (X190).*

A similar situation might exist in tuberculosis in which the patchy distribution of tubercles might lead to a false-negative biopsy. Therefore, it should be recommended that pleural biopsy be repeated whenever necessary. Nevertheless, analysis of the clinical course of 6 of the 9 patients with a biopsy diagnosis of nonspecific fibrosis did not seem to justify the continued suspicion of tuberculosis or neoplastic disease. As indicated in Table 3, patients who, before biopsy, were suspected of having neoplastic involvement of the pleura have had a subsequent clinical course suggesting that no evidence of neoplastic disease of the pleura has developed. Likewise, in Cases 16 and 17 (Table 3), in which tuberculosis was considered before biopsy, subsequent reanalysis and follow-up observation have suggested that 1 patient, who was a drug addict, had a pulmonary infarction, and the other, who had a recent steering-wheel injury to the sternum, had a post-traumatic hemothorax with pleural fibrosis. Nevertheless, these patients are being closely observed.

In 2 of the 9 patients the pleural effusion was superimposed on other known serious disease, and tuberculosis was considered to be possibly coexisting. Case 11 (Table 3) had rheumatic carditis without clinical evidence of congestive heart failure, but with frequent attacks of atrial and ventricular arrhythmia. He had a recurrent pleural effusion, which at first had the characteristics of a transudate, but later protein, cell content and specific gravity increased. After one year this patient succumbed to his disease, and autopsy confirmed the nonspecific nature of the pleural effusion. The other patient (Case 12, Table 3) had Hodgkin's disease, and an infiltrate of the right lower lobe, with pleural effusion, developed. Tuberculosis had to be considered. The pleural fluid was an exudate, and did not contain any malignant cells. Cultures were negative. Autopsy three months later disclosed Hodgkin's disease involving the lung, but the pleura showed only nonspecific fibrosis.

This procedure was especially useful in distinguishing the various sources of pleural effusion in patients with lymphoma. Pleural effusion in this group may occur as a result of lymphomatous involvement of the pleura (Case 8, Table 3) or as a result of obstruction of lymph channels by the lymphoma (Cases 12 and 13, Table 3) or by postirradiation fibrosis. It may, finally, be caused by a second disease such as tuberculosis (Case 3, Table 3).

DISCUSSION

Neoplasm, infections and congestive heart failure are the three most important groups of diseases that may cause a pleural effusion. Among the infections, tuberculosis and bacterial pneumonia are most common. Pleural effusion may occur in a variety of other diseases — for example, pulmonary infarction, trauma, disseminated lupus erythematosus, glomerulonephritis and cirrhosis of the liver. In a recently published analysis of 436 patients with pleural effusion, Leuallen and Carr[1] found that the detection of malignant cells and the isolation of micro-organisms from the fluid provided the most important diagnostic clues. Nevertheless, in 75 of the 436 patients no definite diagnosis could be established despite the use of the diagnostic facilities of a large medical center. This points to the need for additional diagnostic technics. Our experience and that of others[14,15] suggest that needle biopsy of the parietal pleura may contribute significantly to the early detection of the cause of a pleural effusion. Although the specimens obtained by us were only subjected to histologic examination, they should also be suitable for bacteriologic studies.

There is an increasing awareness of a significant incidence of tuberculous pleural effusion in older people.[16] The need for the early diagnosis of a curable disease in such patients in whom the presence of a pleural effusion frequently indicates neoplastic involvement, cannot be overemphasized. Robertson[16] found that 8 of 216 consecutive patients with primary tuberculous effusion were over fifty years of age. One of our patients was sixty-four years old (Case 4, Table 3).

In 1 patient with bronchogenic carcinoma and pleural effusion needle biopsy of the pleura showed only nonspecific fibrosis. This indicates that needle biopsy does not necessarily provide a representative

sample of the diseased pleura. Tubercles and metastases may be distributed on the pleura in a patchy fashion, and the pleura may respond to these implants by a marked desmoplastic reaction. The biopsy needle, therefore, may not reach the characteristic pathologic tissue. Since the technic of biopsy is simple and without undue risk, if the recommended precautions are heeded, it is advisable that the procedure be repeated in doubtful cases. Katz, Donohoe and Mathews[15] have recommended that the needle biopsy be followed by a biopsy taken at thoracotomy, whenever the clinical suspicion of serious disease persists after inconclusive needle biopsy. It should be stated that there are pitfalls even in this surgical method as shown in M.P. (Case 1, Table 3) of this study, who was initially subjected to this operative procedure but in whom tissue obtained consisted only of fibrin. Subsequent needle biopsy disclosed a caseating granuloma.

None of the 6 living patients with the histologic diagnosis of fibrosis has had tuberculosis or any other chronic infection, and in all but 1 the pleural effusion has disappeared during the observation period of four to ten months. Although a probable diagnosis has been made in these patients they are being closely observed.

Summary and Conclusions

Needle biopsy of the parietal pleura is a simple procedure without undue risk. The technic is described.

This report deals with the first 20 patients who were subjected to this procedure. The histologic diagnosis was caseating granuloma in 5 cases, malignant neoplasm in 4 and nonspecific fibrosis in 9, and in 2 an insufficient specimen was obtained.

Needle biopsy of the parietal pleura appears to be a useful technic in the differential diagnosis of pleural effusion.

We are indebted to the Department of Medical Illustration and Photography of the West Side Veterans Administration Hospital for assistance in the preparation of this paper.

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PLEURAL BIOPSY*

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IN 1953 Sutliff, Hughes and Rice[1] reported a series of 21 cases of pleural disease presenting various problems of management and diagnosis. Pleural biopsy in 17 cases showed granulomatous disease of the pleura compatible with the diagnosis of tuberculosis. Three cases showed neoplastic invasion of the pleura, and in 1 case yeast organisms identified as agents of North American blastomycosis were found. No mention was made whether these were consecutive cases or whether they were selected cases showing positive findings. The technic was one of open pleural biopsy. A portion of rib was resected, and the pleura exposed through an incision in the periosteum.

Since that time DeFrancis, Klosk and Albano[2] have reported 2 cases of tuberculous pleural effusion diagnosed by Vim–Silverman needle biopsy. This was done when free pleural fluid existed. From the biopsied portion of parietal pleura, typical granulomatous lesions were demonstrated. Small and Landman[3] presented 5 cases of open pleural biopsy utilized as an aid in the diagnosis of a pleural effusion of undetermined etiology and in each case described the presence of granulomatous lesions in the parietal pleura.

At the moment it appears that 24 cases have been reported in which pleural biopsy has established a

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definitive cause of tuberculous effusion. In addition, Sutliff et al.[1] have shown that the technic has value in demonstrating the invasion of carcinoma into the parietal pleura.

The concept that tuberculous pleural effusion arises from a subpleural focus that has ruptured into the intrapleural space is gaining wide acceptance. On the average, 60 to 70 per cent of patients with idiopathic pleurisy with effusion, if inadequately treated, have clinical tuberculosis within five years.[4] There is evidence that in almost every untreated case of tuberculous effusion active pulmonary disease will ultimately develop.[5] If a pleural effusion is assumed to be tuberculous the patient is committed to long-term chemotherapy, after which a definitive diagnosis of tuberculosis may never be made. In the original series of Sutliff et at.[1] only half the cases were found to contain tubercle bacilli on culture examination of the pleural fluid. In many cases the physician first sees the patient after the effusion is absorbed and when only a blunted costophrenic angle remains.

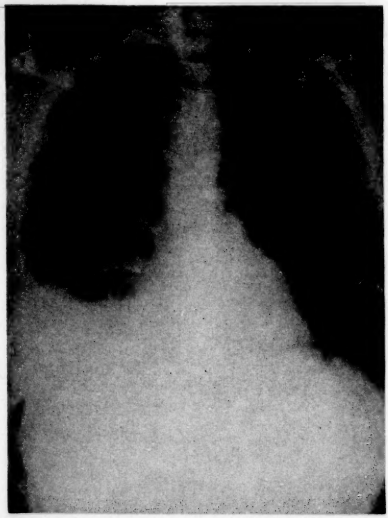

FIGURE 1. *X-Ray Appearance of a Typical Case of Residual Pleural Fibrosis after Acute Tuberculous Pleurisy with Effusion.*

The initial pleurisy with effusion occurred a year and a half before biopsy. In the interim the patient had had three evaluations of the blunted costophrenic angle without a diagnosis.

To date we have found no evidence that consecutive cases of pleural effusion or blunted costophrenic angle or both (Fig. 1) have been studied by open biopsy. We undertook a study of such cases with a *history of pleurisy with effusion,* to determine the accuracy of pleural biopsy in establishing the cause. In some cases clinical evaluation had established a nontuberculous lesion before biopsy.

The Pulmonary Disease Center at the 3275th USAF Hospital, Parks Air Force Base, is a diagnostic center for chest problems for the entire Air Force, and in addition is directly responsible for all chest diseases occurring in a resident population of 4000 to 8000 enlisted men and 8000 permanent personnel and their dependents. We are presenting 16 consecutive cases studied by the methods of Vim–Silverman needle biopsy and open pleural biopsy. The patients ranged in age from two to forty-seven years.

TABLE 1. *Results of Pleural Biopsy in 16 Cases.*

Final Diagnosis	How Established	Diagnostic Biopsy		Biopsy Noncontributory
		Case diagnosed on histology only	Cases with acid-fast bacilli found by stain or culture	
Tuberculous pleurisy, with effusion	Pleural biopsy	4	5	
	Subsequent positive sputum			1
Traumatic hemothorax	History of trauma, with rib fracture	0		1
Thymic cyst	Thoracotomy	1		0
Effusion due to streptococcal pneumonia	Bacteriologic & serologic evidence	0		2
Carcinoma	Pleural biopsy	1		
Bilateral effusion of undetermined origin		0		1
Totals		11	5	5

TECHNIC

The first 5 patients in our series with pleural effusion were examined by needle and open biopsy technics under local anesthesia. The open biopsy was no more difficult and tissue specimens obtained were so superior that the needle biopsy method was abandoned. The pleura is approached through an intercostal incision, which is carried through intercostal muscles and endothoracic fascia to the pleura. The pleura is cleaned by blunt dissection, and the visible portion grasped with an Allis forceps and excised. Experience has taught us that the most consistent and easily accessible point where the parietal and visceral pleura are fused is through the seventh or eighth interspace in an anterolateral position on the involved side. In most cases fusion in this area occurs as early as six weeks from the onset of the effusion, but a free pleural space does not contraindicate the biopsy even though a pneumothorax may result. Immediate catheter suction is instituted, and the patient is usually not even aware that his lung has collapsed.

There were no other complications. In cases of tuberculous involvement of the pleura, the gross appearance of the pleura is suggestive of the final diagnosis, but a thin, glistening pleura may still be the site of granulomatous disease. The patients were ambulatory on the day of surgery, and there was no change in the x-ray appearance of the lungs in any of our cases.

In each case a portion of the fresh specimen was taken for bacteriologic study, which included preparation of direct smears and search for fungi, tissue

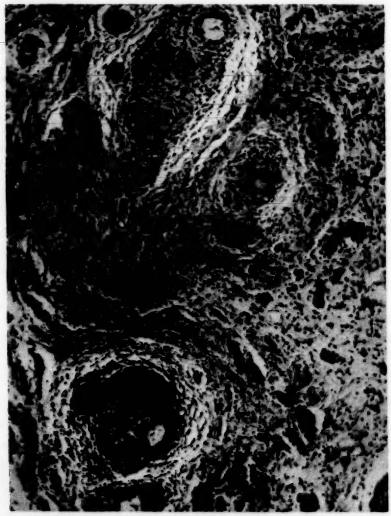

FIGURE 2. *Tissue Section of Pleural Tissue Obtained from the Patient in Figure 1, Showing Typical Granulomatous Lesions with Langhans Giant Cells.*

digestion and concentration and preparation of smears for acid-fast bacilli, as well as culture on Petrogani's medium, Sabouraud's agar, thioglycollate broth and blood agar. The remaining tissues were then fixed in formalin, and sections were stained with hematoxylin and eosin. In all cases showing granulomatous lesions in the routine sections, further sections were cut and stained with Kinyoun's carbol fuchsin and by the periodic acid-Schiff reaction. Two observers carefully examined these sections for organisms.

RESULTS

The results of pleural biopsy in the 16 cases are shown in Table 1.

Nine of the 16 cases showed typical small granulomas of little more than miliary size (Fig. 2). They were composed of masses of epithelioid cells surrounded by zones of fibrosis. Langhans-type giant cells were numerous in all cases. Caseous necrosis was not conspicuous; small foci of necrosis were found in about half the cases. The granulomas and the surrounding tissues showed a marked infiltration with lymphocytes.

Careful search of the carbol-fuchsin-stained sections revealed acid-fast bacilli in only 2 of the 9 cases, and these numbered only 3 to 5 per section. Both yielded positive pleural-fluid cultures for tubercle bacilli. Three cases in which tubercle bacilli were not recovered by any other means yielded growth of tubercle bacilli on *culture of the parietal pleura.* In the other cases presenting the histologic picture of tuberculosis no organisms were ever obtained. No fungous growth was found in any case. In 1 case with a normal pleura on biopsy after four months of antituberculous chemotherapy, cavitation of the left lung, with a positive sputum, developed six months later;

FIGURE 3. *Pleural Effusion, the Result of Extension to the Pleura of Mucinous Adenocarcinoma in a Twenty-seven-Year-Old Man Believed to Have Granulomatous Disease.*

in this case the previously blunted costophrenic angle had disappeared, leaving a sharp angle at the time of biopsy. These 10 patients all had positive tuberculin reactions, and other skin tests for fungous diseases were variable.

One patient was a twenty-seven-year-old man in whom x-ray studies had demonstrated a solitary circumscribed pulmonary lesion in 1953 that had been diagnosed elsewhere as a granuloma (Fig. 3). A

massive pleural effusion developed in 1955. Studies of bronchial secretions, sputum and pleural fluid were negative for acid-fast bacilli, fungi and tumor cells. Pleural biopsy demonstrated well differentiated, mucin-producing adenocarcinoma (Fig. 4).

A two-year-old girl had a cystic tumor of the thymus that occupied the entire right hemithorax.* Pleural biopsy in this case showed only dense fibrous tissue without epithelial elements. Nevertheless, the procedure disclosed a large cystic space within the chest containing 250 ml. of clear fluid, and a diagnosis of cystic mass of the chest was made before thoracotomy.

Two cases of pleural effusion were diagnosed before biopsy as streptococcal pneumonia. In both a significant rise in the antistreptolysin titer was observed. These illnesses occurred during a local epidemic of streptococcal disease. Pleural biopsy in these 2 cases yielded fibrous tissue showing minimal

FIGURE 4. *Tissue Section of the Parietal Pleura Obtained by Biopsy in the Case in Figure 3, Demonstrating Invasion by Adenocarcinoma.*

or no infiltration with inflammatory cells. Cultures were negative. In neither did the biopsy contribute to the establishment of a diagnosis.

One case presented as a blunted costophrenic angle, apparently the result of hemothorax after a nonperforating injury to the chest. There was x-ray evidence of rib fractures. The biopsy specimen showed only fibrous tissue.

In a case of bilateral effusion with blunted costophrenic angles, the biopsy specimen showed connective tissue with a superficial zone of infiltration with lymphocytes, plasma cells and eosinophils. There were no giant cells or foci of necrosis. The picture was that of inflammatory disease; the histologic findings did not suggest an etiologic agent. The diagnosis in this case is probably diffuse collagen disease on clinical grounds, since the tuberculin skin test and all fungous skin tests were repeatedly negative.

*This case is reported in detail elsewhere.

DISCUSSION

The technic of open pleural biopsy seems to offer a useful and accurate method of diagnosis. In 10 suspected cases of tuberculous effusion, granulomatous lesions were found in 9 cases. Postpneumonic pleural thickening or effusion does not appear to produce granulomatous changes in the pleura, nor do the residua of traumatic hemothorax. In 2 cases of intrathoracic neoplasm a diagnosis was made or substantiated when other diagnostic technics had failed. In our hands the procedure biopsy carries no morbidity, and is of such value that we recommend it in every case of pleural effusion or blunted costophrenic angle in which the cause is not established by ordinary clinical methods.

It is axiomatic that pleurisy with effusion in a young tuberculin-positive person, without antecedent bacterial pneumonia or evidence of other underlying disease, must be considered tuberculous and so treated. The physician always has some reservations about committing these patients to long-term antituberculous therapy. Histologic evidence of granulomatous disease before institution of chemotherapy has been reassuring to us.

We confirm the observation that tuberculous pleural effusion represents actual granulomatous disease of the pleural membranes and not a so-called allergic reaction. The source of pleural contamination seems to be invasion of the pleural space by organisms from an active subpleural focus.

It has been noted that bacteriologic diagnosis in cases of pleurisy with effusion is often difficult.[6] In the present series organisms were demonstrated in only 5 of the 9 biopsy specimens with histologic evidence of tuberculosis, despite a careful search of appropriately stained sections and smears and the inoculation of cultures in all cases. In active tuberculous lesions of the lung, especially those untreated by drugs, acid-fast bacilli are ordinarily demonstrated easily. The difficulty in demonstrating organisms in the biopsy specimens may reflect the small amount of tissue removed for study. We believe that the disease represents true pleural contamination because organisms were demonstrated in 5 cases, the histology in the other 4 cases was entirely similar to that in those 5, and the histology is indistinguishable from naturally occurring or experimental tuberculous infection found anywhere in the body.

Our program of chemotherapy is adjusted to follow present-day standards for the treatment of active minimal pulmonary tuberculosis, even when we do not demonstrate actual parenchymal disease by x-ray or sputum examination.

When there is a possibility that a pleural effusion is due to neoplastic invasion of the pleural membranes the biopsy technic is extremely valuable in determining operability.

Summary

Sixteen consecutive cases of pleural effusion or blunted costophrenic angle submitted to open pleural biopsy are presented, and a technic of open pleural biopsy without the necessity of rib resection is described.

In 9 out of 10 cases in which tuberculous pleural effusion was suspected the diagnosis was confirmed by the finding of typical histologic evidence of tuberculosis in the specimen. Acid-fast bacilli were demonstrated in 5 of the 9 specimens.

Two cases of intrathoracic neoplasm are described in which the diagnosis was established as a result of pleural biopsy.

Two cases of streptococcal pneumonia with effusion, one case of residual hemothorax and 1 case of collagen disease in which the biopsy showed no specific changes are included.

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THE ANALGESIC PROPERTIES OF NUMORPHAN (14-HYDROXY DIHYDROMORPHINONE)*

A New Synthetic Narcotic

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SINCE the discovery of morphine a ceaseless effort has been made to improve its somnifacient and analgesic effects, and at the same time to decrease the undesirable reactions. In the past fifty years many drugs with morphinelike activity have resulted from these efforts. Some of these drugs resemble morphine and are modifications of the naturally occurring alkaloids; others are produced synthetically. Numorphan (14-hydroxy dihydromorphinone hydrochloride),§ a synthetic derivative of the alkaloid morphine (Fig. 1), differs from Dilaudid by the addition of a hydroxyl group at the fourteenth position — a change that is purported to increase its analgesic properties.[1] It differs from codeine and its congeners by the absence of a methoxy group in the alpha ring.

Patients and Methods

Two hundred patients between the ages of four and eighty years were studied. Doses of Numorphan between 0.5 and 20 mg. were given subcutaneously, with an average dose of 1 mg. The double-blind procedure was employed to determine the equivalent dosage of Numorphan to morphine and Demerol.[2]

All patients had neoplastic diseases and were under strict hospital surveillance. Fifty-one patients received 1 mg. of Numorphan, with 0.4 mg. of atropine sulfate as a preoperative medication. Ninety-five patients received the drug in the postoperative state. The remaining 54 patients received it for comparison

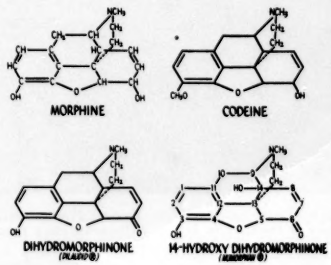

FIGURE 1. *Schematic Formula of Numorphan (14-Hydroxy Dihydromorphinone) Compared with Those of Morphine, Codeine and Dilaudid.*

The major change from Dilaudid is the hydroxyl group at the 14 position.

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§Kindly supplied by Endo Products, Incorporated, Richmond Hill, New York.

with other narcotics, during the course of their illness.

Results

Over nine thousand doses of the new drug were administered by the parenteral route to 200 hospital patients. A double-blind test on 8 patients showed that a dose of 2 mg. of Numorphan was equivalent to 16 mg. of morphine sulfate, 100 mg. of meperidine (Demerol) or 4 mg. of dihydromorphinone (Dilaudid).

The majority of patients in this series had previously received medication for relief of pain. The initial dose of Numorphan that afforded satisfactory relief of pain was 1 or 2 mg. Occasionally, 3 mg. was required initially to comfort the patient completely.

The first effects were felt within five to eight minutes of a single subcutaneous injection, and the full influence of the drug was usually experienced within ten to twenty minutes. Subjectively, the initial action was one of conscious comfort and increased body warmth, with indifference to slight noises and discomfort; sleep and the desire to sleep were induced

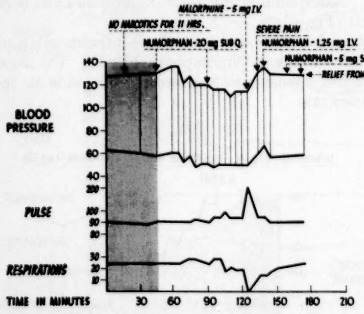

FIGURE 2. *Changes in Blood Pressure, Pulse and Respirations after the Subcutaneous Administration of Two Successive Doses of 20 Mg. of Numorphan to a Fifty-four-Year-Old Man (a Narcotic Addict) with Multiple Myeloma.*

Note the respiratory depression without much change in pulse rate, and the prompt response to Nalorphine, necessitating a repeated dosage of Numorphan for relief of pain. The patient weighed 60 kg.

smoothly and uneventfully. Despite increasing doses the patients usually could be easily aroused and remained co-operative during the conscious state.

No untoward reactions or side effects were noted in single doses up to 10 mg. There was no loss of tactile sensation. Nausea and vomiting and constipation were not observed. One patient (A.R.N.), a woman with a past history of cholecystitis, repeatedly experienced cramplike pains in the right upper quadrant fifteen to twenty minutes after receiving morphine or Dilaudid. This was attributed to the sphincter-contractive properties of these alkaloids. She was completely asymptomatic on 2 mg. of Numorphan.

Among the 51 patients who received 1 mg. of the new drug with 0.4 mg. of atropine sulfate as a preoperative medication, no untoward events attributable to the medication were observed during the anesthesia and surgical procedures. Postoperatively, in 95 cases, the pain-relieving action of Numorphan was rapid and afforded three to six hours of effective analgesia that could be maintained with continued regular use at these intervals.

Toxicity

Respiratory or pulse depression was minimal, even with doses up to 5 mg., in patients who were not debilitated. In patients who were dependent on narcotics doses of 10 mg. resulted in no toxic symptoms; in 2 such patients, administration of 20 mg. did not cause toxic manifestations. However, in the debilitated state, the administration of 5 mg. produced respiratory depression. K.O.T., a fifty-five-year-old woman, had an extensive carcinomatosis due to an ovarian neoplasm. After an emergency laparotomy for bowel obstruction, 0.5 mg. of Numorphan was ordered every two to four hours, but this dose was reduced because of her extremely weak, depressed condition. The patient inadvertently received 5.0 mg. When seen about twenty-five minutes later, she was cyanotic, and the respirations were 3 or 4 per minute. Nalorphine, 5 mg., intravenously caused an instantaneous response, the respirations increasing to 15 per minute and the color promptly improving.

Increasing the dose up to 20 mg. in the narcotic-dependent patient failed to cause any consistent respiratory or blood-pressure changes. The injection of 40 mg. within a period of forty-five minutes in the addicted patient caused marked respiratory depression, necessitating Nalorphine (Fig. 2), S.T.R., a fifty-four-year-old man with far-advanced multiple myeloma, had been dependent on narcotics for twelve months. He required exceedingly large doses of morphine, Dilaudid, Pantopon and Numorphan for relief of pain. On July 23, 1954, he received two 20-mg. doses of Numorphan within forty-five minutes and was studied carefully for changes in blood pressure, pulse rate, temperature and respirations (Fig. 2). The first 20 mg. was administered eleven hours after the previous medication. The patient at this time was suffering from severe generalized bone pain. The pain became tolerable within twenty minutes, and complete comfort was achieved within thirty minutes of the initial 20 mg. The main pharmacologic changes observed were hypotension (blood pressure of 136 systolic, 70 diastolic, to 120 systolic, 58 diastolic) and miosis. The second 20 mg. was administered fifteen minutes later (forty-five minutes after the initial 20 mg.). A nadir of the hypotension

was observed transiently twenty minutes later at a pressure of 110 systolic, 60 diastolic, with a rise to 118 systolic, 60 diastolic, and the pulse became thready. The administration of Nalorphine, 1 ml., precipitated severe withdrawal symptoms. The blood pressure promptly rose to 130 systolic, 70 diastolic, the pain returned in all its fury, and an additional 11 mg. of Numorphan was required for relief.

noted. There was a rise in temperature of 1°F. in 2 patients. There was a transient depression in the pulse and blood pressure in 4 patients, with a prompt return to normal (Table 1).

The most marked physiologic effects were observed in the remaining patient, a sixty-three-year-old, debilitated woman weighing 42.2 kg. (93 pounds), who received a single intramuscular injection of 5 mg. A

TABLE 1. *Maximum Changes after the Administration of 5 Mg. of Numorphan to 5 Women.*

NAME	WEIGHT	AGE	CHANGE IN RESPIRATIONS	CHANGE IN TEMPERATURE	CHANGE IN BLOOD PRESSURE		CHANGE IN PULSE
					SYSTOLIC	DIASTOLIC	
	kg.	yr.	%	°F.			
P.A.R.	61.2 (135 lb.)	34	−20	+0.4	−16	− 4	+12
K.A.R.	43.5 (96 lb.)	44	−25	+1.4	− 8	− 4	+18
K.O.R.	50.3 (111 lb.)	45	−25	+0.2	−18	−20	+ 6
G.R.O.	57.2 (126 lb.)	49	−35	+1.0	−10	− 2	+20
M.G.R.	42.2 (93 lb.)	63	−36	+0.4	−68	−32	+10

ADDICTION LIABILITY

In no case did the discontinuance of the drug appear to be a problem of addiction either after its short use in the average preoperative and postoperative patient or in similar transient employment. Prolonged administration in this study, however, was virtually limited to patients who had previously received one or more other narcotics in abundance. Most of these patients were already dependent on narcotics.

Too few patients without previous narcotic experience were studied to warrant a conclusive opinion concerning addiction. There can be no doubt, however, that the prolonged administration of Numorphan represents considerable addiction liability. The tentative impression was gained that the addictive properties of this drug lay between those of morphine and Dilaudid. Furthermore, Numorphan could effectively be substituted for other narcotics in dependent patients. The withdrawal syndrome could also be precipitated by N-allyl normorphine in patients on Numorphan. Additional evidence of addiction liability can be derived from the specific counteraction of respiratory depression induced by the new drug. Further data are needed, however, to determine the rapidity, tenacity and sequelae of the addiction. Addiction-liability tests are being made by Dr. Harris Isbell under the auspices of the Committee on Drug Addiction and Narcotics, Division of Medical Sciences, National Academy of Sciences, National Research Council.[3]

PHARMACOLOGIC DATA ON ACUTE ADMINISTRATION

Five patients who had not received any narcotics before the study received 5 mg. of Numorphan intramuscularly (Table 1). In 2 of these patients, a depression in respiratory rate of 20 to 36 per cent was sustained depression of the respiratory rate resulted and was soon followed by an accompanying hypotension. Nalorphine at this point rapidly nullified both effects (Fig. 3).

One volunteer was given a single intramuscular injection of 10 mg. of Numorphan (Fig. 4). The main significant change was a transient depression in respiratory rate.

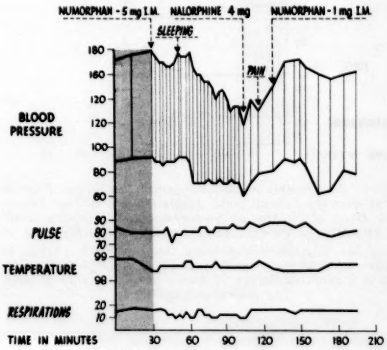

FIGURE 3. *Excessive Hypotension after 5 Mg. of Numorphan Intramuscularly, Necessitating the Administration of Nalorphine, with Prompt Recovery, in a Sixty-three-Year-Old Debilitated Woman with Hodgkin's Disease (the Weight Was 42 Kg.).*

Post-mortem examination in 10 cases gave no evidence of damage to the liver, spleen, kidney, lungs or nervous system that could be attributed to the drug.

Prolonged Administration

One patient, L.E.R., a forty-two-year-old woman, with far-advanced metastatic papillary adenocarcinoma of the ovary, received 6516 mg. of Numorphan over two hundred and forty-five days. She had previously been addicted to Demerol and morphine. Substitution of the new drug for these narcotics was carried out repeatedly, without untoward reaction.

Another patient (S.T.R.), a confirmed morphine addict, was studied continuously for ninety-nine days, during which Numorphan, in effective, pain-relieving doses, was alternated with other narcotics administered in effective doses. Whereas, at first, extremely low doses were capable of controlling his discomfort (approximately 5 mg. of Numorphan, equivalent to 50 mg. of Pantopon), he subsequently required much larger amounts. Just before his death, from the eighty-fourth to the ninety-sixth day of the study, he required between 40 to 70 mg. of Numorphan per day, which is equivalent to approximately 100 to 150 mg. of morphine (Fig. 5).

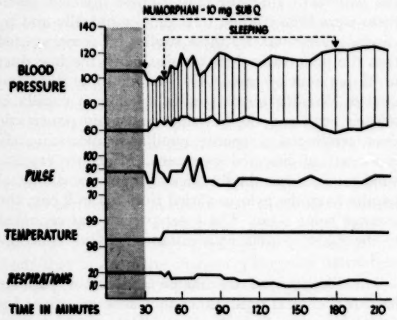

Figure 4. *Minor Changes in Blood Pressure, Pulse, Temperature and Respirations after the Intramuscular Injection of 10 Mg. of Numorphan to a Forty-three-Year-Old Man with Basal-Cell Carcinoma of the Skin Who Was in Good Condition and Weighed 74 Kg.*

Discussion

Numorphan was found to be a potent analgesic in mice by the subcutaneous route.[1] Despite its enhanced analgesic properties (fifteen times those of morphine or two and a half times those of dihydromorphinone) its toxicity was only one and a half times that of morphine and three tenths that of dihydromorphinone. Therapeutic indexes were as follows: morphine, 125; dihydromorphinone 160; and Numorphan 1370. No cumulative toxicity and no significant pathologic or hematologic changes were encountered over prolonged periods of administration.

Numorphan was found to exert prompt morphine-like activity in both narcotic-dependent patients and those without any narcotic experience. The lack of untoward gastrointestinal reactions permitted its extensive and beneficial employment in patients with various neoplastic diseases of the gastrointestinal system in the past two years. During this period it has become the narcotic of choice for *short-term* preoperative or postoperative occasions.

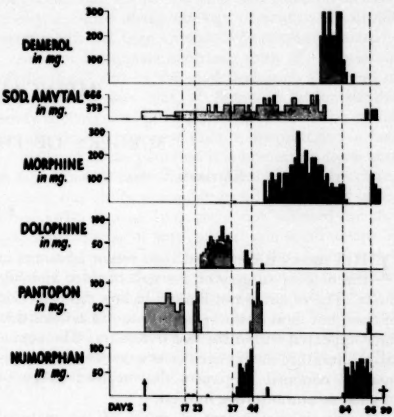

Figure 5. *Comparison of the Effective Dosage of Numorphan and Those of Other Narcotics Required to Afford Relief of Pain to a Fifty-four-Year-Old Man with Far-Advanced Multiple Myeloma (Weight, 60 Kg.).*
Note the increasing requirement for Numorphan within the first six weeks of the study.

The major precaution that must be exercised, as with all narcotics, is the question of addiction liability. These studies were limited to an exploration of the immediate analgesic properties. The chemotherapeutic index of Numorphan is larger than that of morphine or Dilaudid. This in itself might encourage the more ready employment of larger doses of Numorphan than with other narcotics and consequently increase the hazard of addiction. No definitive data were obtained concerning the addictive properties of the drug other than the realization that they are considerable and that the material should not be employed for prolonged periods until the characteristics of addiction are fully defined.

Summary

Numorphan (14-hydroxy dihydromorphinone), a synthetic narcotic, was found to be a promptly effective analgesic in doses of 1 to 5 mg. in 200 patients with neoplastic diseases.

It proved to be an efficient preoperative medication, especially in combination with atropine, in pa-

tients with cancer without addiction to narcotics. No untoward side effects were observed within the dose range of 1 to 5 mg. Absence of nausea, vomiting and constipation was notable.

Despite large doses (6 to 20 mg.) and prolonged administration to patients with cancer addicted to other narcotics, idiosyncrasy was not encountered in any age group.

The addictive properties of Numorphan did not appear to be less than those of morphine or Dilaudid, and more experience in this regard is desirable.

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MEDICAL PROGRESS

SURGERY OF THE BILIARY TRACT*

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THIS survey is concerned with recent advances in the field of surgery of the gall bladder and bile ducts. The report is not limited to any rigid interval of time, but most of the references are to articles that have appeared within the last five years. The cumulative literature in this area is so extensive that comment is confined to papers that seemed to be of original or authoritative interest.

In editorial assessment of much of the material referred to in this communication we have drawn upon our own clinical experience for comparison.

Anatomy

An excellent book by Michels[1] contains a fine description of the anatomy of the liver and biliary system. It details some of the controversies that revolve about the nature of the ampulla of Vater, the incidence of a common pancreatobiliary channel and the sphincteric mechanism of the pancreatic and biliary ducts. This book contains an elaborate descriptive atlas based upon the personal analysis of numerous anatomic dissections performed by the author.

Pancreatobiliary-Duct Junction

With increasing clinical interest in the anatomic, physiologic and pathologic features of the pancreatobiliary ductal system and the sphincter of Oddi, numerous articles are appearing relative to this field.

In 200 dissections Millbourn[2] investigated the anatomy of the excretory ducts of the pancreas and their relation to each other and to the bile ducts and duodenum. He occluded the papillary orifice by special suture technique and thereafter injected 20 per cent barium sulfate solution into the bile duct or the pancreatic duct, or both. These injected specimens were then studied roentgenographically and by careful dissection. By these studies he demonstrated that the pancreatic duct terminated in the bile duct in 85 per cent of cases. The common bile duct and duct of Wirsung terminated in a common papilla in 5.5 per cent, and the bile duct and main pancreatic duct terminated in separate papillae in approximately 9 per cent of dissected specimens. Millbourn emphasized the fact that the distance of the major duodenal papilla from the pylorus varied from 5.5 to 9 cm., the average being 8 cm. The lesser papilla was cephalad to the major papilla at a distance varying from 0.9 to 3.5 cm.

The locations of the major and minor papillae have real clinical significance in gastric resections for posterior penetrating ulcer in which these ducts may be injured and in the presence of biliary disease such as fibrosis of the sphincter of Oddi and impacted common duct stones, and in transduodenal exploration of the pancreatic ducts. The location of the greater duodenal papilla (papilla of Vater) can usually be made with the duodenum intact, by the careful mobilization of the duodenum and head of the pancreas and subsequent palpation by compression of the lateral duodenal wall against the head of the pancreas. The papilla of Vater can be palpated as a firm papillary projection well down in the second part of the duodenum. The general tendency in searching for the papilla either with or without duodenotomy is to assume an anatomic position much more cephalad than it actually is. With the duodenum open the papillae can be identified by palpation more readily than by inspection. The lesser papilla is more difficult to palpate, but with increasing experience it too can be identified as a firm, small papillary projection approximately 2 cm. cephalad to the major papilla.

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Sterling[3] has made an intensive study of the termination of the common bile duct and the duct of Wirsung. In cadaver specimens the common bile and pancreatic ducts were injected with pigmented gelatin solutions. The specimens were subsequently dehydrated and cleared. These specimens were then studied by photographic and roentgenographic methods, and measurements were made of all specimens under the dissecting microscope. In a group of 100 specimens the terminations of the common bile and pancreatic ducts were observed to fall into four normal categories: completely separate orifices, 42 per cent; common channel starting in distal third of papilla, 38 per cent; common channel starting in middle third of papilla, 14 per cent; and common channel starting at proximal third of papilla, 3 per cent (in 3 per cent only one orifice was identified). In 36 (60 per cent) of 61 cleared specimens the common bile and pancreatic ducts merged. This common channel varied from 0.1 to 1.2 cm. in length. It was found that in 75 per cent the common channel traversed only the distal third of the papilla.

Sterling emphasized the fact that the common concept of an ampulla of Vater is not borne out by this analysis. Both the common bile and pancreatic ducts taper as they pass through the papilla of Vater. An actual ampulla or dilated common termination of the two ducts was seen in only 2 of these specimens. He also stressed the point that although separate channels were present for the common and pancreatic ducts in 42 per cent of these specimens, this observation did not necessarily imply that the remaining 58 per cent of specimens had a common channel that would permit intraductal reflux. He believed that the nature of the sphincteric mechanism was such that a common channel traversing more than two thirds of the papilla was the only type that could permit intraductal reflux. Sterling concluded, therefore, that in only 3 per cent of these cases did such a reflux occur normally between the common bile and pancreatic ducts.

A common objection to this type of analysis based upon cadaver specimens treated with a variety of fixative and clearing agents is the questionable reliability of assessing the presence of a common functional channel. Although we have not analyzed this problem statistically it has been our observation in exploring the pancreatic ducts transduodenally that the duct of Wirsung frequently opens either on the inferior margin of the major duodenal papilla or 2 to 4 mm. within the orifice. This distance would be well within the limits of the sphincter muscle. The chief difficulty in studying the possible role of reflux of bile into the pancreatic ducts by way of a common channel is that if these studies are made primarily on the basis of anatomic dissection, particularly on cadavers or fixed specimens, these relations may be distorted; if, on the other hand, they are made by injection of contrast mediums directly into the common duct, the hydrodynamics of the physiologic mechanism may likewise be distorted. It is possible that cumulative experience with intravenous cholangiography will help delineate the role of reflux of bile into the pancreatic ducts. In approximately 800 such studies at the Lahey Clinic the pancreatic ducts have not been visualized in any cases.[4] Although it is not particularly pertinent to this discussion it has long been our impression that the common-channel theory in terms of the etiology of acute and chronic pancreatitis has been considerably overemphasized.

Another interesting anatomic study of the relation of the distal end of the choledochus to the head of the pancreas was that of Smanio.[5] Although this study is concerned primarily with the relation of the distal end of the common duct to the posterior surface of the head of the pancreas it is interesting to observe that in these dissections the distal end of the choledochus was easily accessible in 60 per cent of cases. Posteriorly, it was frequently not covered by any pancreatic tissue, or was covered to a small extent by a lingula of pancreatic tissue. From the clinical standpoint it is more important to realize the relation of the anterior wall of the distal common bile duct to the head of the pancreas. Doubilet and Mulholland[6] have studied extensively the relation of the biliary and pancreatic ducts, primarily in reference to their investigation of pancreatitis.

Oral Cholecystography

Two carefully analytical studies of oral cholecystography with iopanoic acid (Telepaque) have recently appeared, the first by Whitehouse[7] and the other by Reynolds and Fulton.[8]

Both these papers attest to the high degree of diagnostic accuracy of Telepaque. Both emphasize the fact that doses of 2 or 3 gm. are adequate in almost all cases and that nonfilling of the gall bladder with 2 or 3 gm. of the dye given orally does not usually require re-examination with a larger dose. Reynolds and Fulton re-examined 90 cases of nonvisualized gall bladders in a series of 1000 examinations by repeating the test with a double dose of contrast medium. In only 4 cases (4.4 per cent) was the gall bladder visualized with the larger amount of iopanoic acid. In all 4 the visualization with a larger dose was of poor density. They repeated the cholecystographic studies in several patients, using smaller doses, and found that such doses gave excellent cholecystographic density.

In the series reported by Whitehouse, 50 of 124 cases showed nonvisualization of the gall bladder. This represented 40.3 per cent of the entire group. Six of these 50 cases with nonvisualization showed opaque or partially opaque calculi. Calcification of the gall bladder was demonstrated in 1. Only 16 of the 50 patients were subjected to re-examination. In 6, repetition of the test with a 2-gm. dose again

showed nonvisualization. In 1 case a 3-gm. dose showed a faint gall-bladder shadow without definite stones. In 9, the repeat examination was done after 4 gm. of the contrast medium was administered, with persistent nonvisualization in 5, a questionably faint shadow in 1, a faint shadow with stones in 1 and a good shadow with stones in 2. Forty-five of the 50 patients, or 90 per cent, with nonvisualization proved to have gallstones at the time of operation. Of 5 patients without stones, 1 had carcinoma of the gall bladder, 1 had carcinoma of the head of the pancreas with a distended gall bladder, 1 had a questionable fistula, the precise nature of which was not described, 1 had hydrops of the gall bladder, with active, chronic cholecystitis, and 1 had slight evidence of chronic cholecystitis. The author concluded that nonvisualization of the gall bladder after the ingestion of 2 gm. of Telepaque confirmed, if possible, by second examination when surgery is contemplated, is definitely indicative of biliary-tract disease.

Faint visualization was noted in 27 cases reported by Whitehouse, or 21.8 per cent of the series. Twenty-one of the 27 patients had demonstrable calculi on the films — 1 opaque, 6 mixed, and 14 lucent. Four of the 27 patients had a repeat study, with demonstration of a good shadow with stones in 1 case, 2 showing no change on re-examination and 1 remaining faint after a 4-gm. dose of Telepaque. Twenty-three of the 27 were eventually demonstrated to have stones. Of the 4 patients without stones, 1 had had a previous cholecystectomy, and the present visualization was of a cystic-duct remnant. One had carcinoma of the head of the pancreas, with active chronic cholecystitis; 1 showed slight, and 1 severe active chronic cholecystitis. Good visualization was reported in 44 cases, or 35.5 per cent, of the group analyzed by Whitehouse. Stones were observed in 42 per cent, and there was a question of a polyp in another. In 1 case no abnormality was suspected, and at operation the gall bladder was grossly normal. The suspected polyp was shown to be a cholesterol stone partially embedded in the gall-bladder wall. In only 3 cases was the visualization considered excellent; in each, stones were observed in the cholecystograms and found at operation.

Although there can be no question of the high diagnostic dependability of cholecystography utilizing Telepaque the precise incidence of diagnostic accuracy can never be determined since many patients who have normal cholecystograms will not have abdominal exploration. Since the positive diagnosis of cholelithiasis is made in only about 15 per cent of the patients studied with the cholecystogram it is probable that the diagnostic accuracy is slightly less than that generally reported.

Reynolds and Fulton emphasize the importance of occasional spot films of the gall-bladder area after the manner advocated by Lubert and Krause.[9] The importance of filming the gall bladder in the upright or lateral decubitus position can occasionally be demonstrated in the patient in whom the clinical history is highly indicative of cholelithiasis and yet the cholecystogram is allegedly negative. The stones may be visualized in layers by means of this technic.

Intravenous Cholangiography

The most significant advance in the study of the biliary tree in recent years concerns the development of an intravenous method of x-ray visualization of the intrahepatic and extrahepatic biliary-duct system. Sodium iodipamide was originally described in Germany.[10-14]

Cholografin, the di-sodium salt of N, N'-adipyl-bis (3-amino-2, 4, 6-triiodo-benzoic acid) is identical with biligrafin, originally employed in Germany. Some of the early clinical reports in this country were recorded by Bell and his associates,[15] Berk et at.,[16,17] Fulton and Sandweiss,[18] Glenn et al.,[19] Orloff and others[20] and, from this clinic, by Wise and O'Brien,[21,22] and McDonough and Wise.[23] In the presence of reasonably normal liver function 10 per cent of the drug is excreted by the kidneys. In the presence of significant liver damage the quantity excreted by the kidneys is in direct proportion to the degree of disturbance in liver function. The concentration of the drug in the bile may be thirty to a hundred times that found in the blood. This high concentration of dye in the excreted bile accounts for the chronologic appearance of the opaque material first in the intrahepatic ducts followed by visualization of the larger hepatic ducts, proceeding to opacification of the extrahepatic ducts and ultimately to a delineation of the gall bladder if this organ is functioning normally. In this respect Cholografin differs materially from the common dyes used for routine oral cholecystography.

Within ten minutes after the intravenous injection of the dye an initial film will usually visualize the hepatic and perhaps the common bile ducts. Subsequent films taken at intervals of ten to twenty minutes will show a gradually progressive increase in density of the dye within the hepatic and common bile ducts, with optimal visualization of the ducts in twenty to sixty minutes. The time relation of filling of the gall bladder is more variable. In analyzing the material from this clinic Wise has noted the gall bladder to be visible in some cases within thirty minutes after injection of the drug, and in others the gall bladder has not been apparent until two hours after the injection.

Sensitivity

Glenn and his associates, reporting 88 administrations of Cholografin to 80 patients, recorded mild reactions in 38.8 per cent and moderately severe reactions in 2 patients, or 2.5 per cent of the series. These authors did not observe any cases of respiratory

or circulatory collapse as reported by Ward[24] and Hornykiewytsch.[12] Shehadi[25] reported side reactions in 16.5 per cent of a group of 200 patients after the injection of Cholografin. Only 1 of these cases showed an allergic reaction with marked drop in blood pressure. Wise and O'Brien,[26] from this clinic, recorded reactions of varying degrees in 34 of 300 patients — a reaction rate of 11.3 per cent. Of the 34 patients who had reactions, skin tests were recorded in 28, and of these, 17 tests were regarded as negative and 11 as positive. An additional 94 skin tests were recorded in the patients who did not have reactions, and in these, 13 were regarded as positive and 81 as negative. Only 1 patient in this series has shown any marked vasomotor disturbance.

Visualization

Visualization of the ductal system was obtained in 255 of 300 injections (85 per cent) reported by Wise. One hundred and ninety-one of these injections were performed in patients who had had a previous cholecystectomy, with visualization in 158 (82.7 per cent). In 109 cases the test was performed on patients who had not had cholecystectomy, and visualization was obtained in 97 (88.9 per cent). In all, the test was performed because of history, physical or laboratory findings indicative or suggestive of diseases of the biliary tract. Wise has repeatedly emphasized the fact that the ductal visualization after study with Cholografin will depend upon the selection of patients. If the test is applied indiscriminately the percentage of visualization will be low; if it is reserved only for patients who are shown to have no jaundice and no depression of liver function visualization will approach 100 per cent. Since it may be precisely the patient with mild jaundice and borderline liver impairment in whom the test will be most helpful it is obvious that too much emphasis can be placed upon the rate of visualization. Although it has been the observation of our group that there is no absolute line of demarcation where the probability of visualization can be uniformly predicted, it is true that there is little justification in attempting this study in patients with a serum bilirubin value above 4 mg. per 100 ml. and in the presence of bromsulfalein retention above 40 per cent.

Indications for Intravenous Cholangiography

The primary indications for intravenous cholangiography are the patient who has had a previous cholecystectomy and has recurrent or persistent symptoms suggestive of biliary-tract disease, patients with nonvisualization of the gall bladder with the oral dye method, certain cases of biliary-tract disease of infants and small children and isolated cases of chronic relapsing pancreatitis.

Interpretation

A comprehensive interpretation of the intravenous cholangiograms must be concerned with visualization of the ducts, size of filling defects, position of filling defects, presence of filling defects, visualization of the gall bladder if it is present, irregularities of the duct itself, the egress of dye into the duodenum, the configuration of the termination of the duct, the persistence of the dye in the ducts and sustained density of the ducts after an elapsed interval when under normal circumstances the density of the dye should be decreasing.

Size of the common duct. Although it is difficult to define the upper limits of the normal diameter of the common bile duct, McClenahan, Evans and Braunstein,[27] in evaluating their material, arbitrarily chose 7 mm., as determined by the examination of a posterolateral projection, employing a 102-cm. (40-inch) target-film distance.

Utilizing this standard these authors found marked dilatation in 9 of 10 common bile ducts in which stones were demonstrated, the average diameter in this group being 15 mm. and the maximal diameter 25 mm. These authors found no constant relation between the size of the common bile duct and the time elapsing after cholecystectomy.

The arbitrary figure of 7 mm. as the upper limit of normal compares favorably with the diameters of the common bile and hepatic ducts as determined by Shehadi, which were made on a group of normal subjects after the administration of iopanoic acid.

In the material analyzed by Wise a wide range in the diameter of the common bile ducts was observed in the 142 patients studied by this method after cholecystectomy. These ducts varied in size from 3 mm. in 4 cases to a maximum of 30 mm. in 1. The commonest diameter observed in this group was 10 mm., which was found in 29 cases. In an attempt to assess the significance of size, the patients who were subsequently operated on were separated into two groups. The first group comprised 36 cases in which the study indicated obstruction of the distal end of the duct. The second group, showing no obstruction, included 32 cases. The diameter of the unobstructed ducts varied from 3 to 15 mm. whereas that of the obstructed group ranged from 8 to 30 mm. There is an area from 8 to 15 mm. in diameter in which there is considerable overlapping of the cases of the obstructed and nonobstructed ducts. All common bile ducts explored and found to be above 15 mm. in diameter were partially obstructed, and all those below 8 mm. in diameter were found to be unobstructed. Since 82 out of 142 visualized common bile ducts after cholecystectomy showed a ductal diameter ranging from 8 to 15 mm. it is apparent that in approximately 57 per cent of cases the mere size of the common bile duct will not permit a distinction regarding the presence or absence of obstruction.

Duration of opacification of ducts. There is a rough correlation between the size of the common bile ducts and the duration of opacification. In the smaller

ducts, up to 8 mm. in size, opacification had frequently disappeared at the end of sixty to ninety minutes after injection, whereas the larger ducts were commonly opacified for two hours or more. Thus, currently, a diagnosis of partial obstruction of the distal end of the common duct is made by our department of radiology primarily upon the observation that the density of the dye in the duct at the end of a hundred and twenty minutes has not been significantly reduced above its maximal density, as generally observed at sixty minutes.

Clinical Application

Intravenous cholangiography promises to be most helpful in demonstrating the presence of partial obstruction of the common bile duct secondary to common-duct stones, fibrosis of the sphincter of Oddi and incomplete strictures of the common bile duct. Frequently, it will be possible for the radiologist to determine the precise cause of the partial obstruction, but at the present stage of development of this technic it is more important that valid criteria be established for the roentgenographic detection of the partially obstructed biliary duct. Since most patients with stricture of the common bile duct will have moderate or severe jaundice, intravenous cholangiography will have limited applicability to this problem. It will be valuable, however, to the extent that it may show a partial stricture in a patient with recurrent bouts of abdominal pain associated with chills and fever and accompanied by mild jaundice. It is precisely this type of patient in whom the diagnosis is difficult to establish.

Effect of drugs. Glenn and his associates[19] observed that morphine or paregoric increased the length of time the common bile duct remained visible, and believed that the administration of these agents had some advantage under certain circumstances. Wise has also observed prolongation of the visualization of opacification by morphine but believes that it should be reserved only for special cases since it eliminates one of the most important factors in evaluating disease of the duct — namely, the length of opacification and the increasing density with the passing of time. The recent observation of a patient who had had a previous sphincterotomy showed the filling of the common bile duct and intrahepatic radicles when the test was done in the conventional manner. There was a mild degree of narrowing of the common duct, presumably at the site at which the cystic duct had been divided, and the test was repeated after the administration of morphine. The subsequent films showed significant dilatation of the hepatic and common bile ducts as compared with those taken without morphine. There was higher density of opacification and more prolonged filling, indicating that in special circumstances the administration of morphine may have some virtue, but emphasizing all the more that its routine use will distort the normal physiologic dynamics of the biliary tract and may lead to misinterpretations or may interfere with some of the more important time and density relations, which can be extremely valuable in detecting partial obstruction of the common duct.

There can be little doubt that intravenous cholangiography is a real contribution to the diagnosis of disease of the biliary ducts. The test must be done with care. It has definite limitations, but with increasing experience in its application and interpretation, more and more valuable information will be obtained as a result of its use.

Cholelithiasis

Although the surgical treatment of cholelithiasis by cholecystectomy has become increasingly popular and progressively safer over the years, it is surprising how frequently patients harbor undetected gallstones and how commonly physicians and surgeons alike will assume a casual attitude regarding the presence of cholelithiasis despite the known hazards. Lieber[28] found gallstones in 9.94 per cent of 34,666 autopsies. The distribution in white females over twenty years of age was 21.7 per cent compared to one incidence of 7.7 per cent in white males. Lieber's statistics showed an increasing prevalence with advancing age. Bartlett and Quinby[29] analyzed 2243 operations performed at the Massachusetts General Hospital for chronic cholecystitis. Cholecystectomy was performed on 1280 patients, and cholecystectomy with choledochostomy on an additional 963. In the 1280 cases in which cholecystectomy was performed, there were 8 postoperative deaths, a mortality of 0.6 per cent. None of the deaths occurred in patients under fifty years of age. Seven of the 8 deaths were due to extra-abdominal complications, 5 resulting from sudden cardiac catastrophes and 2 from massive pulmonary emboli. One fatal case was related to intra-abdominal infection. There were 17 deaths in the 963 cases in which cholecystectomy with choledochostomy was performed, a mortality of 1.8 per cent. In this group 2 of the patients who died were under fifty years of age.

These authors emphasized the fact that the mortality was three times as great after cholecystectomy with choledochostomy as after cholecystectomy alone. In this group of patients in whom choledochostomy was combined with cholecystectomy, the mortality was essentially the same when the common duct failed to yield stones as when stones were present and removed. In the recent series reported from this clinic by Colcock and McManus[30] concerning 1356 patients, the mortality was 1.1 per cent. Included in this series were 72 patients with acute cholecystitis and 62 patients who had had a previous cholecystectomy. The mortality after cholecystectomy alone was 0.9 per cent, as compared with a mortality of 1.1 per cent in patients who had cholecystectomy and choledochos-

tomy combined. Further analysis of the records of 435 patients who had combined cholecystectomy and choledochostomy shows that there were 3 deaths in 119 patients with common-duct stones, a mortality of 2.5 per cent, and 2 deaths in 216 patients in whom the common bile duct was explored but no stones were found.[31] The mortality in this group of patients with negative exploration of the common duct was 1 per cent. In 1 of the 2 patients who died after a negative choledochostomy there was an associated pancreatitis characterized by areas of fat necrosis and edema. The common bile duct in this case was dilated and thickened.

This statistical comparison of the patients operated upon at the Lahey Clinic showing a comparable mortality for cholecystectomy combined with choledochostomy and for cholecystectomy alone has been a consistent feature of periodic analyses of this problem in previous reports from the Clinic. The fact that no significant increase in mortality has attended combined cholecystectomy and choledochostomy as performed here appears to justify our conviction that the clinical indications for exploration of the common duct should be kept sufficiently broad to minimize the possibility of overlooking common-duct stones.

Acute Cholecystitis

The probable basis for the continued controversy between early and delayed operations for cholecystitis may be found in a comparison of the material reported by Meagher and Campbell[32] and by Glenn and Wantz.[33] The data presented by Meagher and Campbell concern a group of patients treated in a large city hospital, whereas those reported by Glenn and Wantz relate to a group of patients observed at the New York Hospital. Meagher and Campbell point out the high mortality that follows gall-bladder surgery performed on an emergency basis. The mortality in 88 cases of acute cholecystitis in their study was 7.9 per cent. The mortality in 36 cases of acute cholecystitis requiring emergency operation was 13 per cent, and that in 52 cases requiring elective procedures was 3.9 per cent. Meagher and Campbell concluded that the material presented in their study emphasized the need for a more conservative approach to the treatment of acute cholecystitis.

Glenn and Wantz advocated early surgical intervention in the treatment of acute cholecystitis. They emphasized the point that early surgery was not necessarily emergency surgery. The patient was first prepared carefully and was brought to optimal condition for either cholecystectomy or cholecystostomy. Glenn and Hays[34] reported a mortality after operative procedures in patients sixty-five years of age and over in acute cholecystitis as follows: cholecystectomy, 6.37 per cent; cholecystostomy, 15.6 per cent; cholecystectomy in combination with choledochostomy, 15.3 per cent — an average mortality in 92 patients of 10.08 per cent. In the presence of chronic cholecystitis in the same age group the mortality was 3.03 per cent for cholecystectomy alone, 27.3 per cent for cholecystostomy, 3.38 per cent for cholecystectomy combined with choledochostomy and 4.3 per cent for choledochotomy. The mean mortality in 225 cases of chronic cholecystitis was 4.4 per cent.

In the group of 1356 cases of cholelithiasis reported from the Lahey Clinic by Colcock and McManus[30] there were 72 patients with acute cholecystitis and 60 with subacute cholecystitis. Common-duct stones were found in 32 of the 132 patients with acute or subacute cholecystitis (24 per cent). Acute pancreatitis was present in 8, and chronic relapsing pancreatitis in 5 patients. Hepatitis, cholangitis and cirrhosis of the liver, singly or in combination, were concomitant findings in 15 of these 132 patients. Six patients had fibrosis of the sphincter of Oddi, and 7 had an associated internal biliary fistula. Eight of the 72 patients with acute cholecystitis showed pericholecystic disease characterized by perforation or abscess formation. Acute gangrenous cholecystitis associated with carcinoma of the gall bladder occurred in 1 case, and 1 patient had a carcinoma of the pancreas with acute cholecystitis. There were 2 deaths in the 132 patients with acute or subacute cholecystitis. One death occurred in a fifty-eight-year-old man who had associated pancreatic necrosis. Cholecystectomy and drainage of the pancreatic abscess was performed. The other death, which occurred in a sixty-five-year-old woman who had cholecystectomy, choledochostomy and transduodenal sphincterotomy, was due to a cerebrovascular accident, with hemiplegia and coma, on the fifth day after operation.

It is difficult to reconcile the divergent points of view regarding early as opposed to delayed operation in acute cholecystitis. It appears that much of this controversy revolves about a consideration of the same disease occurring in different strata of the population. The greatest mortality apparently occurs in acute cholecystitis in patients treated upon an emergency or semiemergency basis in large city hospitals in which the hospital population frequently includes patients who are less well nourished and who delay unduly admission to the hospital. The advocates of early operation are more commonly found among surgeons dealing principally with private patients. It has always seemed to us that the fervor of the controversy is out of proportion to the relative merits of either side. Frequently, it is difficult to determine what an early operation is, since these patients are admitted to the hospital at widely varying intervals after the onset of the acute attack. It has been our practice to pursue no rigid dictum for either early or delayed operation. Rather, we have preferred to treat each case on its individual merits. We do not regard acute cholecystitis as an emergency in the sense that these patients are ever operated upon in the middle of the night or immediately upon admis-

sion unless free perforation is recognized or suspected. It seems advisable to prepare all these patients in terms of restoring the fluid and electrolyte balance and correcting blood-volume deficiency before operation is performed. The survey of the cardiovascular and renal status of the elderly patients and the determination of the status of glucose metabolism are extremely important. When acute pancreatitis is suspected of complicating acute cholecystitis it is our tendency to delay operation until the acute pancreatitis has subsided or evidence of pancreatic sepsis has become apparent.

We prefer, for the most part, cholecystectomy in the treatment of acute cholecystitis, recognizing nonetheless that simple cholecystostomy may prove life saving in the rare case of the patient who is an extremely poor risk. We do not believe that patients who have had acute cholecystitis should be discharged from the hospital to return for interval cholecystectomy unless there is some decisive contraindication to surgery during the initial admission.

(To be concluded)

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MEDICAL INTELLIGENCE

PAROXYSMAL NOCTURNAL PORPHYRINURIA*

Heretofore Undescribed Manifestation of Chronic Porphyria

JOSEPH A. SMITH, M.D.,† AND
ABRAHAM M. FRUMIN, M.D.‡

PHILADELPHIA

PORPHYRIA is a relatively uncommon metabolic disorder that has engaged the interest of many investigators. The protean manifestations have led to a classification of the various types as seen in clinical practice.[1,2] We have recently observed a form of chronic porphyria characterized by the paroxysmal nocturnal nature of the porphyrinuria. Observations on the possible mechanism of these findings are presented along with the clinical and biochemical determinations.

CASE REPORT

R.G., a 43-year-old Negro, was admitted to the Nazareth Hospital on July 17, 1955, because of the voiding of "bloody urine" in the morning on arising. He had noticed this for the past 2 months and further stated that his urine became lighter as the day progressed. The past medical history was noncontributory except for an appendectomy and cholecystectomy in 1943. He had been employed as a foreman in a dress factory for the past 27 years, smoked a package of cigarettes daily and was a moderate drinker. The family history was irrelevant. A review of the systems elicited the information that he had noticed increasing pigmentation of the skin for the past 2 months. This was particularly prominent over the cheeks, forearms and abdomen. Before admission, penicillin was given for the red urine, and giant hives and angioneurotic edema subsequently developed. Also before admission, sodium bicarbonate, aspirin, phenobarbital, triple sulfonamides and various other proprietary medications had been given.

Physical examination revealed a well developed, well nourished man who weighed 86.2 kg. (190 pounds) and was in no acute distress. The examination was entirely noncontributory except for areas of pigmentation and scaling on the cheeks, forearms and abdomen.

The temperature was 99°F., the pulse 70, and the respirations 20. The blood pressure was 124/70.

Examination of the blood showed a red-cell count of 5,080,000, with a hemoglobin of 15.6 gm. per 100 ml. (100 per cent), hematocrit of 48 per cent, mean corpuscular volume of 98 cubic microns, color index of 1.0, reticulocytes of 0.5 per cent, platelets of 280,000 and white-cell count of 5800, with 3 per cent band forms, 60 per cent segmented neutrophils and 37 per cent lymphocytes. The blood smear showed slight anisocytosis, poikilocytosis, hypochromia and minimal polychromatophilia. No abnormal red or white cells were seen. Platelets were abundant. The blood sugar was 98 mg., the blood urea nitrogen 14 mg., and the serum bilirubin 0.9 mg. per 100 ml. Cephalin flocculation was negative, and thymol turbidity was 1 unit. A bromsulfalein test showed no retention of dye after 30 minutes. A blood Wassermann test was negative, as was a sickling preparation. Urinalysis disclosed a red color with an alkaline reaction. The specific gravity was 1.005, with negative tests for albumin and sugar. The sediment contained occasional white cells. X-ray films of the chest, gall bladder, common bile duct and kidneys were normal.

The more pertinent findings were in his urine, which was deep red when he arose and which became lighter as the day progressed. This persisted throughout his entire hospital admission and subsequent 6-month observation period, despite cessation of all medication. Analysis of the urine showed a marked excess of uroporphyrin (700 microgm. per 100 ml.) and a considerable increase of coproporphyrin (62.5 microgm. per 100 ml.). No porphobilinogen was found at any time.

The attacks of red urine could be precipitated if the patient was kept in a recumbent position after the urine had become normal in color. It was noted that the next voided specimen was again deep red. Apparently, there is a postural or orthostatic component to this syndrome since it can be reproduced at will by a change to a horizontal position.

DISCUSSION

The increasing pigmentation of the skin associated with light sensitivity, the urinary findings and the protracted course of the patient's illness all support the clinical diagnosis of chronic porphyria. The initial presumptive diagnosis of paroxysmal nocturnal hemoglobinuria (Marchiafava–Micheli syndrome) was excluded by the the absence of anemia, reticulocytosis, hemoglobinuria and hemosiderinuria. The paroxysmal nocturnal nature of the porphyrinuria, never before described, is particularly emphasized. Since this phenomenon can be readily reproduced if the patient is placed in a recumbent position, an orthostatic or postural component of this syndrome is postulated. The increased renal blood flow occurring with the change of body position may be one factor in determining the presence of excessive porphyrins in the urine.

SUMMARY

A case of paroxysmal nocturnal porphyrinuria is reported.

The orthostatic or postural component for urinary porphyrin excretion is stressed.

The determinations of urinary porphyrin were performed through the assistance of Dr. Cecil J. Watson, professor of medicine, University of Minnesota Medical School, Minneapolis.

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CURRENT CONCEPTS IN THERAPY*

II. Sedative-Hypnotic Drugs — Chloral Hydrate

CHLORAL hydrate, introduced into medicine by Liebreich[1] in 1869, has long been and still is one of the most effective and least expensive of the sedative-hypnotic drugs. Furthermore, when used wisely, it has very little toxicity. It is frequently the favorite of the dermatologist since skin reactions from it are uncommon. The psychiatrist often finds it the agent of choice since it is much less likely to produce mental excitement than hypnotics of the barbiturate variety. The general practitioner likes it because the dose can be readily adjusted to the patient's needs and it is an excellent agent when used in conjunction with an analgesic. It can be given to patients of all ages and physical status. Patients with cardiac disease tolerate it well. There is no proof that it is deleterious to the heart in therapeutic doses.[2]

Undoubtedly, chloral hydrate deserves to be used more than at present. It is a rapidly effective hypnotic, sleep being produced in ten or fifteen minutes. It seldom causes excitement and usually gives deep, quiet sleep for five to eight hours. No hangover or aftereffects are observed, and addiction is exceedingly rare. It is therefore excellent to use in patients exhibiting insomnia of Types 2, 3 and 4. Frequently, it is a useful adjunct to analgesic therapy when sedation or sleep is desired.

Chloral hydrate after absorption is converted to trichloroacetic acid and trichloroethanol. The depressant hypnotic effect is entirely due to trichloroethanol. The kidney excretes any trichloroacetic acid not changed to trichloroethanol, and the liver detoxifies trichloroethanol by conjugating it with glucuronic acid. The resulting urochloralic acid is excreted by the kidney.[3] It should be noted that this nonhypnotic substance is capable of giving a false-positive test for sugar. Because of its mode of detoxification it is not wise to use large amounts of chloral hydrate in patients with liver or kidney damage. In the presence of liver disease it is generally better to avoid its use.

Although chloral hydrate is one of the least expensive of the sedative-hypnotic drugs, the need to prescribe it as a liquid, capsule or suppository frequently makes its cost to the patient more than that of the barbiturates and approximately that of the newer nonbarbiturate drugs. It should not be combined with other sedatives or analgesic drugs, and preparations of it containing bromides should be abandoned in therapy.

*Prepared under the supervision of the *Journal's* Committee on Advertising.

Most patients are sedated by a dose of 0.25 to 0.5 gm., but for more effective sedation or hypnosis a dose of 1.0 to 2.0 gm. is better. Occasionally, a dose of 3.0 gm. is needed. Although it takes about 10 gm. to cause death, it has, in feeble patients, done so in a dose of 5.0 gm. Toxic doses severely depress respiration.

Chloral hydrate can be administered as a 10 per cent solution dissolved in water and given in doses of 1 or 2 teaspoonfuls with milk or fruit juices. It is very inexpensive when given in this fashion, but it is bitter, creates a burning sensation on the mucous membranes of the mouth and causes gastric irritation. Some of the bitterness can be disguised by prescribing it in conjunction with various syrups such as Coca-cola, orange and citric acid. A favorite prescription of this type is as follows:

Chloral hydrate	12 gm.
Syrup of citric acid	50 ml.
Water, to make	120 ml.

Label: 1 teaspoonful dissolved in half a glass of fruit juice.

Chloral hydrate can be given by rectum. A retention enema containing the dose, usually 1 or 2 gm. dissolved in olive oil, is satisfactory. It is also available as a palatable sugar-free elixir (Somnos) containing approximately 0.25 gm. per teaspoonful, capsules of 0.25 and 0.5 gm. and rectal suppositories containing 0.65 and 1.3 gm.

Although these preparations are improvements over aqueous chloral hydrate, they are capable of causing mucous-membrane irritation, gastric distress and rectal irritation. This frequently leads to the selection of another agent. There is still a definite need for a palatable nonirritating preparation of chloral hydrate.

An interesting recent development in chloral hydrate therapy has been the preparation and introduction of the pentaerythritol derivative of chloral (Periclor). The powder has a bitter taste, and the capsules on standing have a strong odor of chloral hydrate. However, it is not very irritating to the mucous membranes. It is supplied as capsules containing 0.3 gm. A dose of 0.3 gm. every six hours is recommended for sedation. For hypnosis 0.6 gm. is advised. There is as yet insufficient clinical experience to indicate whether this preparation has any advantage over chloral hydrate.

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CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 42411

PRESENTATION OF CASE

A fifty-two-year-old man entered the hospital because of dysphagia.

One week before admission an episode of nonradiating subxiphoid and substernal pain occurred while he was playing golf. Five days before entry he noted some difficulty in swallowing. The next day there was increasing dysphagia associated with subxiphoid pain. Subsequently, he was able to swallow only liquids. There was no hematemesis or melena.

FIGURE 1. *Roentgenogram of the Barium-Filled Esophagus, with Two Zones of Stricture in Its Distal Portion (Arrows). There are several tiny projections of barium from the distal zone of the esophageal narrowing.*

When he was three and a half years old, a gastrostomy was performed at another hospital allegedly because of two strictures in the lower portion of the esophagus. For a year or two after retrograde dilatation of the esophagus swallowing was normal except for occasional temporary difficulty if a large piece of food was not thoroughly masticated.

Physical examination showed a well nourished man in no distress. The heart was not enlarged. A Grade 1, apical, systolic murmur was audible.

The temperature was 98.2°F., the pulse 92, and the respirations 18. The blood pressure was 156 systolic, 104 diastolic.

The urine was normal. Examination of the blood revealed a hemoglobin of 15.5 gm. per 100 ml. and a white-cell count of 10,400. X-ray films of the barium-filled esophagus demonstrated two zones of stricture in the distal third (Fig. 1): a relatively short zone of narrowing in which the lumen did not distend more than 1 cm. was present 12 cm. above the diaphragm; below this there was a 4-cm. length of relatively normal-appearing esophagus distal to which was a long, narrowed area extending to the level of the cardia where the lumen was reduced to about 5 mm.; several tiny projections from the proximal end of this latter zone of narrowing were noted.

An operation was performed on the sixth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM BROWN*: X-ray films of the barium-filled esophagus taken shortly before admission show two areas of stricture (Fig. 1). One is rather short and located about 12 cm. above the diaphragm in the region of the ninth thoracic vertebra. Below this is a segment, about 4 cm. long, of relatively normal esophagus with pliable walls and apparently intact mucosal pattern. Extending from the lower margin of the normal area down to the esophagogastric junction is a tubular stenotic area, about 5 or 6 cm. in length, in which the mucosa is altered. The stenotic lumen opens not more than 5 mm. There is evidence of ulceration, as manifested by the small match-head-sized niches in the esophagus anteriorly. Another interesting finding is the soft-tissue indentation against the air-filled cardia of the stomach at the esophagogastric junction. That may or may not be significant. The x-ray examination was done at another hospital, and apparently no further films were taken at this hospital.

The initial symptom of pain in the substernal areas that began suddenly and increased in severity over the ensuing five or six days immediately brings to mind a number of diagnoses, including myocardial infarction, ulceration of the duodenum, stomach and

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esophagus, possibly hiatus hernia, with gastritis of the herniated portion of the stomach, and cardiospasm. The field of possibilities is narrowed somewhat by the dysphagia, which followed the pain by about two or three days and which also progressed in severity to the point that the patient was able to swallow only liquids by the time of admission. I note that he had a Grade 1, apical, systolic murmur and a diastolic blood pressure of 104. I assume that the hypertensive cardiovascular disease was incidental and unrelated to the principal disease. The difficulty, I judge from the films, symptoms and history, was clearly located in the esophagus.

Hiatus hernia, I think, can be excluded after a look at the films; there is no evidence of herniation of the stomach above the diaphragm. Instead, there is a rigid stenotic area in the esophagus that is constant on all the films.

Cardiospasm can cause acute distress in the substernal area and dysphagia. Again, the films exclude this possibility. The picture of cardiospasm — a dilated pliable esophageal wall above a spastic cardiac area — is diametrically opposed to the one seen in this case.

Reflux esophagitis in the presence of an acute gastritis and hyperacidity may produce exactly these symptoms. The finding of a narrowed esophageal lumen in the lower esophagus is against reflux esophagitis but does not exclude it.

Another possibility, which I hesitate to mention, is scleroderma. Characteristically, the wall of the scleroderma tous esophagus is rigid and the lumen dilated. A greater portion of the esophagus is usually involved in the process; ulceration is not common, and, by the time the esophagus is involved, there are other clinical manifestations, specifically the changes in the skin.

Several neoplasms may involve the lower esophagus. Intrinsically, it may be involved by adenocarcinoma or squamous-cell carcinoma of the fungating or infiltrating scirrhous types. The lower esophagus may be affected by various types of extrinsic tumors. If this is tumor, it is quite clearly not fungating and would fit better into the infiltrating scirrhous type.

A simple fibrotic stricture, secondary to an old caustic burn, will produce the picture of a rigid, stenosed, lower esophagus. An ingested caustic is apt to produce localized strictures higher in the esophagus as well. The patient had a childhood experience that resulted in strictures of the lower esophagus, gastrostomy and retrograde dilatation. These strictures may have been caused by ingestion of a caustic. Other mechanisms can affect a stricture of the esophagus at the age of three and a half, but the most common is the swallowing of a caustic. With the treatment by retrograde bougienage of the lower esophagus he had almost, but not complete, restoration of normal swallowing function. He had no pain and only insignificant and infrequent dysphagia when he swallowed coarse or badly chewed boluses of food. In other words, this man had an esophageal stricture of minor proportions for about forty-eight years, presumably secondary to a caustic stricture in childhood. The disease was not a current episode of only one week's duration. During this time he had had no pain and only rarely dysphagia. Accepting this fact — the findings in the films are compatible with an esophageal stricture — I must then ask what suddenly precipitated the pain.

It could be postulated that he had swallowed a large, rough bolus of food that irritated the mucosa and produced ulcerations. Ingestion of a foreign body could have done the same thing. A more likely cause, and the one upon which I intend to base my diagnosis, is that a neoplasm developed in the site of the esophageal stricture. This neoplasm must have been of a scirrhous infiltrating type, which invaded and destroyed areas of esophageal mucosa and produced ulcerations. The occurrence of neoplastic disease in the site of old scarring is a fairly familiar disease complex. A number of cases have been reported. It is entirely possible for such a neoplasm to exist in an esophagus without giving evidence of hematemesis or bleeding in the stools. The ulcerations are very small.

To correlate this with the x-ray findings, the lower end of the esophagus shows stricture formation with ulcerations and destruction of the mucosa. As I mentioned before, the possibility that a soft-tissue mass is bulging into the gastric portion of the cardia suggests that a paracardial lymph node is involved by neoplasm. That is an ancillary finding that may or may not actually have been present but is certainly suggested on one film.

DR. AUSTIN L. VICKERY: Dr. Benedict, have you a comment?

DR. EDWARD B. BENEDICT: I am inclined to agree with Dr. Brown. I think the patient could have had reflux esophagitis with a great deal of stenosis, but I do not think that he did have it. I think that there was a stricture, probably produced by lye, and there is a good chance that a cancer developed.

About fifteen years ago I reported[1] 2 cases of carcinoma developing in benign strictures: one was a lye stricture, and the other was a congenital stricture. Of course, there may have been a foreign body within the esophagus or just a sudden inflammatory process with fibrosis.

DR. VICKERY: We have certainly seen more than an occasional case of carcinoma many years after a lye stricture.

DR. BENEDICT: I found 33 cases reported in the literature.

DR. VICKERY: I think that that possibility was thought of here, particularly in view of the hospitalization during early childhood. We tried to find out if the patient had swallowed lye, but he could not recall that when he was questioned by the clinicians.

DR. BENEDICT: Did he have an esophagoscopy?

DR. VICKERY: He did not have an esophagoscopy.

The preoperative impression was that he had a stricture, possibly inflammatory, and there was also some question in Dr. Richard H. Sweet's mind whether or not he had a short esophagus, with a hiatus hernia.

Clinical Diagnosis

Stricture of esophagus.
? Short esophagus and thoracic stomach.

Dr. William Brown's Diagnoses

Stricture of esophagus, produced by caustic.
Carcinoma, superimposed on old stricture.

Anatomical Diagnoses

Abortive congenital esophagotracheal fistula (fifty-two-years' duration).
Chronic esophagitis, with stricture formation.

Pathological Discussion

Dr. Vickery: At operation there was no evidence of hiatus hernia, but two inflammatory strictures of the esophagus were found, one about 2.5 cm. and the other about 15 cm. above the cardia, corresponding to the x-ray appearance. Dr. Sweet, in his operative note, remarked that the striking and unexpected finding was that the distal esophagus was atrophic and narrow in diameter and looked characteristically like the segment of esophagus in cases of achalasia. A complication and incidental aspect of the case was that an active ulcer with stenosis was discovered in the first portion of the duodenum, and Dr. Sweet elected to do a pyloroplastic procedure to obviate any possible obstructive complications and to ensure a good result from the esophageal resection. A transthoracic esophagectomy was then performed with an infra-aortic esophagogastrostomy.

The segment of esophagus that we received showed the area of narrowing at the cardiac end. The lumen of the constricted zone was markedly narrowed, and the wall was greatly thickened and fibrotic. There was a tiny area of dimpling on the mucosa overlying the stricture, which proved to be the opening of a small, fistulous tract leading into the scarred portion of the wall and terminating in an intramural cystic space, a little over 0.5 cm. in diameter, that was filled with thick yellow fluid. Microscopically this tract was partially lined with squamous epithelium and communicated with a cyst in the muscularis lined with pseudostratified ciliated epithelium. In the region of this respiratory-epithelium-lined cyst, there were fragments of cartilage and glands of typical tracheal origin (Fig. 2). These surprising microscopical findings suggest an interesting phenomenon that we do not recall having seen before. We interpret these to be the result of a congenital esophageal abnormality — namely, an abortive or incomplete tracheoesophageal fistula with subsequent scarring. How else one might account for actual segments of normal trachea, incorporated with the esophageal wall, would be difficult to imagine.

Although over 90 per cent of all cases of congenital esophageal atresia correspond to Type C in the figure (Fig. 3), according to Gross,[2] a small percentage of deformities fall into the category depicted in Type E (Fig. 3), in which there is a continuous esophageal lumen associated with a tracheoesophageal fistula. It

Figure 2. *Photomicrograph of the Esophagus, Showing the Fistulous Tract* (A), *Cartilage* (B) *and Cyst* (C).

seems reasonable that the case under discussion represents a basic developmental defect of this type, but with an incomplete fistulous tract between esophagus and trachea. This anomalous fixation of esophagus and trachea undoubtedly produced enough deformity and distortion of the esophageal lumen to have caused the symptoms of esophageal obstruction, dating back almost fifty years in this patient. This chronic, mechanical obstruction was complicated by secondary inflammatory changes with scarring, serving slowly to aggravate the stricture process.

I asked Dr. Earle W. Wilkins, Jr., yesterday whether Dr. Sweet had ever had a case like this before, and he said that he could not recall one; I have been unable to find a record of similar cases, although there surely must be some.

Dr. Alfred Kranes: How do you account for

the patient's acute symptoms on the basis of what you found?

DR. VICKERY: I do not think we can. Dr. Sweet did comment in the note that the musculature above the area was very well developed, and it is probable that the patient had some type of spasm; otherwise, I do not know. It seems to me that in many types of esophageal narrowing one cannot always relate the suddenness of an acute obstructive episode to the pathologic process, which often appears to have been present a long time.

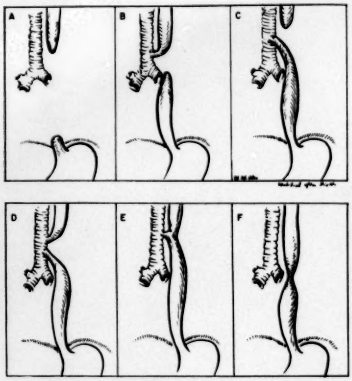

FIGURE 3. *Drawing Adapted from Gross.*[2]

DR. BENEDICT: You do not think that there was reflux esophagitis with spastic stenosis?

DR. VICKERY: There was chronic inflammation and esophagitis in the narrowed segment, but no frank ulcerations.

DR. BENEDICT: If an esophagoscopy had been done and a biopsy had shown cartilage, the esophagoscopist would certainly have been embarrassed.

DR. VICKERY: One last thing to mention is that there was another nodule of dense, fibrous tissue with chronic inflammation in the peripheral tissue of the cardia, which probably accounted for the little indentation that Dr. Brown suggested might have been produced by metastases in a lymph node in the paracardial area.

DR. FREDERICK M. TOMCHIK: Is the base of the aberrant tissue in the cardia?

DR. VICKERY: I do not know; there had been so much scarring and shortening in this area that it is difficult to be certain what the original status was.

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CASE 42412

PRESENTATION OF CASE

A seventy-two-year-old man entered the hospital because of hematuria.

Two weeks previously there was an episode of painless hematuria. A second episode occurred a week before admission. There were no other urinary signs or symptoms or loss in weight.

Physical examination revealed a well nourished man in no distress. The edge of the liver was palpable 3 fingerbreadths below the right costal margin. Immediately below the liver and extending from the right flank to almost the mid-line was a soft, ill defined mass that did not descend with inspiration and measured about 10 cm. in diameter. Rectal examination showed a firm prostate that was smooth and not enlarged.

The temperature was 98°F., the pulse 72, and the respirations 20. The blood pressure was 170 systolic, 90 diastolic.

FIGURE 1. *Retrograde Pyelogram, Showing a Large, Rounded Mass in the Right Upper Portion of the Abdomen, with Inferior Displacement and Compression of the Renal Calyxes.*

The urine was normal; a culture of the urine from the bladder showed no growth; cytologic examination for malignant cells was unsatisfactory. Examination of the blood revealed a hemoglobin of 13.4 gm. per 100 ml. The nonprotein nitrogen was 40 mg. per 100 ml. X-ray films of the chest showed moderate cardiac enlargement in the region of the left ven-

tricle; the right costophrenic sulcus was blunted. An intravenous pyelogram demonstrated a rounded mass about 10 cm. in maximal dimension that was continuous with the inferior margin of the liver and extended to the inferior margin of the third lumbar vertebra; this was subsequently shown by pyelography to represent a portion of the kidney that was enlarged; the renal contours on the right could not be adequately traced; there was some delay in excretion of the dye by the right kidney; dilated calyxes were demonstrated in the lower lateral aspect of the renal mass, and subsequently a dilated renal pelvis was outlined; not all the minor calyxes were demonstrated, and the right ureter was not adequately delineated; there was a smooth, rounded mass that measured 8 cm. in maximal dimension within the bladder; the left kidney was normal and excreted the contrast substance promptly. A retrograde pyelogram showed the gross distortion on the right previously described (Fig. 1). Cystoscopic examination was negative.

On the eighth hospital day an operation was performed.

Differential Diagnosis

Dr. Victor A. Politano*: The most likely causes of painless hematuria in a man of this age are bleeding from the prostatic urethra caused either by benign prostatic hypertrophy or carcinoma, tumor of the bladder and renal neoplasm in that order of frequency. Obviously, there are many other causes of hematuria. May I see the x-ray films?

Dr. Joseph Hanelin: The plain film of the abdomen shows a rounded mass in the right upper portion whose inferior margin only can be traced. It is inseparable from both the renal and hepatic shadows, and a normal renal outline is absent. The left kidney is unremarkable in gross appearance. Good function is present on the left; a normal pyelogram was obtained on this side. On the right excretion is delayed. In films taken two and a half hours after the intravenous injection, there is visualization of a mildly distended renal pelvis and of dilated inferiorly displaced infundibula and calyxes. It may be that only the most inferior calyxes are visualized, and there is considerable question whether there is any filling of the middle and superior calyxes. A large, smooth, filling defect is present within the inferior portion of the bladder occupying the major portion of this structure. The right ureter is never well shown, and there may be some obstruction at the ureteropelvic junction. The left ureter shows upward hooking as it enters the bladder. A retrograde pyelogram taken the same day provides little additional information. The renal pelvis on the right is actually not as well filled as in the intravenous study (Fig. 1). The mass in the right upper portion of the abdomen is most probably intrinsic to the kidney. Its smooth outline favors the presence of a cyst over a solid tumor, with the latter possibility not excluded. The filling defect of the bladder could result from a greatly enlarged prostate or an intrinsic lesion of the bladder.

Dr. Politano: The rectal examination revealed a firm, smooth prostate of normal size. This suggests to me that carcinoma of the prostate is not a consideration. I interpret that the word firm is used in distinction to hard. Bleeding from carcinoma of the prostate is usually a late manifestation, and frequently other symptoms suggestive of metastatic disease become evident before bleeding occurs.

Benign prostatic hypertrophy is not entirely ruled out by the rectal findings. There may be considerable intravesicular enlargement of the prostate, which may not be felt on rectal examination. The x-ray films show a large filling defect over the area of the bladder, with hooking of the left lower ureter. These findings are consistent with an enlarged prostate. If the filling defect represented intravesicular enlargement of the prostate, I doubt if ureteral catheterization could have been done.

Cystoscopic examination was negative. This rules out a neoplasm of the bladder or extravesicular compression producing what appears to be a filling defect in the x-ray films. If an extravesicular mass was producing distortion or compression of the bladder, the cystoscopy would not have been reported as negative. Thus, attention is called to the region of the kidney. I am impressed by several findings. The large renal mass appears smooth and suggests a large cyst. The lower calyxes function, but the upper group is not visualized. The renal pelvis fills without filling the upper infundibulum and suggests an obstruction here and at the ureteropelvic junction. The ureter is not visualized in the intravenous or retrograde pyelogram. Likewise, the upper infundibulum is not filled in the retrograde pyelogram. This suggests either that there was an obstruction in the upper infundibulum or that the quantity of contrast medium used was too small. However, one would expect that some medium would have entered the infundibulum. The obstruction could have been caused by nonopaque stones, tumors, inflammatory lesions and so forth. The lesion in the upper pole of the kidney more strongly suggests a cystic mass than a solid tumor. A papillary carcinoma of the upper infundibulum seems to explain most of the symptoms and gross findings. This could account for the painless hematuria; gradual obstruction to the upper pole would explain the development of a large hydronephrotic sac. Tumors seeding at the ureteropelvic junction or ureter would explain the apparent obstruction at the ureteropelvic junction and failure of the ureter to be visualized. It is possible that there was bleeding into this upper pole to increase further the size or actually to produce the obstruction with blood clots.

*Assistant urologist, Massachusetts General Hospital.

The filling defect over the bladder observed in the x-ray films has not been explained. This may have been caused by a blood clot or gas in the rectum. I do not think that there is any lesion producing this defect.

My diagnosis is malignant lesion involving the upper infundibulum of the right kidney, producing obstruction with hydronephrosis and possibly hemorrhage into the upper pole. The lesion was most probably a papillary carcinoma, though a squamous-cell or renal-cell carcinoma invading the infundibulum could produce the same picture.

Clinical Diagnosis

Papillary carcinoma of kidney.

Dr. Victor A. Politano's Diagnoses

Papillary carcinoma of kidney.
Hydronephrosis.

Anatomical Diagnoses

Papillary cystadenocarcinoma of kidney.
Pyelonephritis, chronic.
Ureteritis, chronic.

Pathological Discussion

Dr. Leonard Atkins: Dr. Suby, will you tell us the opinion on the ward and describe the findings at operation?

Dr. Howard I. Suby: Hematuria associated with a firm mass in the right flank suggested a carcinoma of the right kidney with secondary obstruction of the ureteropelvic junction. The expectation was that the carcinoma would be of the papillary type.

At operation when the kidney was exposed it was very firm and could be moved only with considerable difficulty. The mass, however, was not covered with dilated veins such as one sees in the usual renal-cell carcinoma; as the dissection was carried farther, it was felt that the mass was partially cystic. Most of the mass was infected urine, together with old blood, and we were not completely sure whether any papillary carcinoma was present or whether the mass was completely secondary to inflammatory change.

Dr. Atkins: The operative specimen included the right kidney and a segment of ureter. The posteromedial aspect of the kidney was involved by a grossly circumscribed cystic tumor that measured 11 cm. in diameter. The pelvis, which was moderately dilated, was not involved by the tumor, which lay at least 1.4 cm. away from it. The cystic lesion was filled with soft, mushy, red-brown material that was adherent to the inner lining. Several projections, each about 1 cm. in diameter, were also attached to the inner surface of the cystic mass. The renal capsule was easily stripped except at several points of adherence to the tumor. In one area of adherence there were several nodules measuring up to 5 mm. in diameter. Elsewhere the cortical surface of the kidney contained several irregularly depressed areas. The

Figure 2.

renal vein was normal. Microscopically, the tumor was a well differentiated papillary adenocarcinoma that showed foci of capsular invasion and compressed the surrounding renal parenchyma (Fig. 2). There was much necrosis with old and recent hemorrhage within the tumor. Other sections of the kidney showed foci of chronic pyelonephritis. Chronic ureteritis was also present.

The New England Journal of Medicine

Official Organ of
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STATE MEDICAL SOCIETY DUES

AN interesting compilation was recently published in the Secretary's Letter of the American Medical Association in relation to the dues currently paid by members of the state medical societies and that of the District of Columbia. The figures, collected by the executive director of the Michigan State Medical Association, indicate a range from the modest $20 per annum levied on society members in Alabama, Ohio and South Carolina to the similarly modest though not entirely comparable dues of $75 in each of the Dakotas, and the $100 extracted from the professional pocketbook in Nevada, whence comes the silver.

The practitioners of Massachusetts who have gradually accustomed themselves to the payment of $35 (which includes a subscription to the *Journal* and membership in the Boston Medical Library) will note that the average is $42.06; also that county-society dues in general range from $20 to $70 depending on the maintenance of an executive office. Such dues, compared with the small change required by the district societies of this colony, indicate one of the advantages of tribal life along the salt rivers of the Massachusetts shore.

Several state societies, however, either touched with the icy finger of chill penury or anxious to keep up with the times in all matters of taxation, have indicated their intention of increasing the annual levy — Alabama from $20 to $50 on the first of next January; Arizona from $60 to $70 effective on the same date, the extra ten dollars to go to the American Medical Education Foundation; Iowa from $60 to $85; Mississippi a gradual step up from $35 to $50, and Ohio from $20 to $25, effective in 1957. These increases will raise the annual average to $45.16 — a tidy sum but not beyond the capacity of most physicians' incomes.

In addition to these relentless budgetary demands certain other states have made effective special and presumably temporary assessments. Connecticut has added $10 to its customary $28 on a voluntary basis for a building addition; Michigan has slapped a one-year assessment of $10 onto its regular dues of $45 for 1956, and Missouri has added the same sum to its dues of $25 for 1957. Nevada has made an additional assessment of $20 for the American Medical Education Foundation; New York has added $10 to its modest $25 for an employees' pension fund, and Utah, for no publicized purpose, has announced an assessment of $20 in addition to its usual $50. Only the two states mentioned, Arizona and Nevada, have earmarked their increases for the American Medical Education Foundation.

Massachusetts appears to be definitely on the conservative side, especially when viewed in the light of labor-union dues, town, state and federal taxes and the bite that is put on the instinctively charitable physician by the dozens of charitable agencies to

which he willingly subscribes. Many, of course, also pay dues to hospital-staff organizations, special societies, associations, colleges and academies, and journals other than those that they receive ostensibly free gratis as part of one or more of these memberships.

Those who in this great Commonwealth protest too vigorously at their relatively modest society dues must do so as a matter of principle or because of the frugality of all New Englanders and those who come in contact with them.

PLEURAL BIOPSIES

TISSUES obtained directly from the site of various types of lesions have always proved to be a most fruitful source of diagnostic material. Unfortunately, they have not always been fully utilized, and this is understandable in situations in which extensive surgical procedures are necessary to obtain the tissue. Surgical biopsies of lymph nodes or of other superficial lesions, however, have long been used as a major source of material for important differential diagnoses. Exploratory punctures of serous cavities or other infected or otherwise diseased sites for fluid or tissue suitable for culture or for histologic examination have likewise helped to unravel puzzling diagnostic problems; they have also been helpful therapeutically in permitting the introduction of therapeutic agents at the site of the lesion. Recently, exfoliated tissues from various secretions or taken deliberately during endoscopic examinations have added a means of obtaining tissues for examination.

Needle biopsies, properly performed and capable of yielding enough tissue for histologic examination, are now becoming commonplace. They have proved most helpful in the differential diagnosis of hepatic diseases, have revealed the varied pathology, both local and systemic, that may be manifested in the bone marrow and, more recently, have been successfully employed in the study of renal diseases.

Elsewhere in this issue of the *Journal* the technic of needle biopsy successfully applied to diseases of the pleura is described. Another paper in this issue advocates open pleural biopsy as a superior procedure. Both technics have revealed specific lesions that, in most cases, were amenable to curative or palliative therapy. Properly applied, they should prove to be useful additions to the diagnostic armamentarium in pleural and pulmonary diseases, as well as in certain systemic diseases. Obviously, the use of the needle biopsy should prove more widely applicable than the open biopsy, which would be relegated to the domain of the thoracic surgeon. More experience with the needle biopsy will be needed to reveal its full usefulness and limitations as applied to pleural lesions.

POSTGRADUATE MEDICAL EDUCATION AND THE NEW ENGLAND POSTGRADUATE ASSEMBLY

No one is more aware than the practicing physician of the axiom that education is a never-ending process. Because of today's highly geared and nearly frantic medical research, he of all others must be concerned over changes in theories and practice that may precipitate the knowledge gained yesterday into tomorrow's obsolescence.

Organized groups, hospitals, clinics, textbooks and medical journals provide ever-increasing opportunities for postgraduate instruction designed to keep the physician abreast of medical progress, but his continuing education is basically a matter of individual responsibility, initiative and conscience.

Innumerable courses of instruction are available to him; the problem, from the physician's point of view, is that of selection and scheduling. The selection is made, generally speaking, on a basis of personal requirements, most of the courses being practical, with enough theory to prepare him for what may come next, including (an inevitable reference in any discussion of postgraduate medical education) what his patients may have discovered in *Reader's Digest*.

Scheduling must take into consideration the hours that he can most conveniently steal away from the patients who depend on him for the very information that he is seeking to acquire.

The annual New England Postgraduate Assembly — the fourteenth — will be held in Boston, October 30 and 31 and November 1; it was omitted last year because of the interim session of the American Medical Association. It offers, as its predecessors did, a variety of practical lectures, panels, symposiums and clinicopathological conferences. There will be ample opportunities for give and take and "curbstone consultations" among the visiting physicians and selected authorities. There will be enough theory to accomplish the objectives of a true educational effort.

The Assembly's dates were well publicized in advance to enable physicians to schedule the meeting with a minimum of discomfort to themselves or inconvenience to their patients. During its three days of concentrated, practical instruction, the Assembly will provide its registrants with an opportunity not only to be brought up to date without interruptions but also to relax, without interruption, between sessions.

The committee in charge of planning and arranging for the Assembly is to be commended for the excellent, well balanced program, which will be found elsewhere in this issue of the *Journal*.

IN PERPETUITY

ON September 12, 1956, the Frank H. Lahey Periodical Room in the Boston Medical Library was

officially dedicated and opened for use. The ceremonies accompanying the dedication of this perpetual workroom, presented to the Library by the staff of the Lahey Clinic in memory of the Clinic's late founder and director, were impressive and appropriately simple. Dr. Arthur W. Allen, president of the Library's trustees, presided, and Dr. Richard B. Cattell, present director of the Clinic, unveiled a portrait of Dr. Lahey that will oversee the room for generations to come.

The name of Frank H. Lahey will, of course, continue to be known through his recorded contributions to medical progress. But by building Dr. Lahey into the institution that is the Boston Medical Library, the staff of the Lahey Clinic has ensured his perpetuation as a man, rather than as a reference. This practical approach to immortality as an accent to his established works is one that would unquestionably have met with Dr. Lahey's approval and recalls the words of Elihu Root:

> The general, the statesman, the man of affairs, all pass away and are forgotten. But to have builded oneself into the structure of these undying institutions, to have aided the development of these priceless agencies of civilization, is to have lived not in vain, but is to have lived in perpetuity. . . .

We understand from the New Jersey Reporter *that the* Louisville Review *will be transferred to Philadelphia, retaining the present name, however, to the close of the present volume, after which a change will be made.*

Boston M. & S. J. *October 16, 1856*

MASSACHUSETTS MEDICAL SOCIETY

TOXIC HAZARDS*

Lead Poisoning Still Occurs†

Although lead poisoning is not now as prevalent as during the first quarter of the century, it is by no means a rare disease. Its occurrence among painters has been greatly reduced by the substitution of titanium oxide pigment for white lead in inside paints. Lead pigments are still used in outside paints, however, and especially as a priming coat for structural steel. The recent boom in road construction in New England has been accompanied by a few cases of lead poisoning among the men engaged in painting the structural steel required for bridges and elevated highways.

Lead is, of course, a major ingredient of solder, type metal and plumbing devices, but the employment of these metals does not ordinarily constitute an important lead-poisoning hazard. Lead is also a common component of bronzes, and it is occasionally added to certain steels. Compounds of lead are used in plastics and insecticides and as antiknock agents in gasoline, as well as in paints.

The most persistent sources of lead poisoning in this area are in storage-battery manufacture, smelting and refining of scrap lead and lead burning. The lead problem in automobile-body manufacture and repair seems to fluctuate. About twenty years ago it was a serious occupational hazard, but was fairly well under control immediately before World War II. Recently, with the dramatic changes in automobile styles, the use of lead in automobile bodies has again become somewhat of a problem. In general the lead dust, produced when excess lead is ground off, is fairly well controlled in the automobile plants, but in repair shops, satisfactory methods of control are more difficult to provide.

Several laboratory procedures are extremely useful in providing aids for diagnosis of lead poisoning. In addition to blood examination, the determination of coproporphyrin in urine and the quantitative determination of lead in urine or blood are very helpful. These tests can all be carried out by several laboratories in the Boston area.

The use of chelating agents in the treatment of lead intoxication is a relatively new development. Citric acid, a relatively weak chelating agent for lead, has been displaced by the more powerful EDTA, which, when administered intravenously, provides a logical and apparently successful treatment for active plumbism. The effectiveness of oral treatment with the same drug has not yet been entirely established.

In view of the diminished use of lead paint for interior surfaces, the continued occurrence of lead poisoning among children is somewhat surprising. Several cases are reported each year in this vicinity, and the experience in some other metropolitan areas is considerably worse than that in Boston.

Hervey B. Elkins
Massachusetts Division of Occupational Hygiene

*This is one of a series of articles published co-operatively by the Committee on Industrial Health and the Panel on Child Health of the Committee on Public Health of the Massachusetts Medical Society. The panel provides liaison with the Massachusetts Chapter of the American Academy of Pediatrics, whose Boston and Worcester Poison Information Centers are activities of the Committee on Accident Prevention.

†From the Committee on Industrial Health, George F. Wilkins, M.D., *chairman*; Henry C. Marble, M.D.; Karl T. Benedict, M.D.; Harriet L. Hardy, M.D.; George E. Morris, M.D.; Albert O. Seeler, M.D.; and Jermyn F. McCahan, M.D.

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Mid-West Medical College, 1934.
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Boston University School of Medicine, 1952.
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Zunder, Morris L., 52 Florence Street, Roslindale.
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Tufts University School of Medicine, 1955.

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Jefferson Medical College, 1949.

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Harvard Medical School, 1951.

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Middlesex University School of Medicine, 1939.
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Harvard Medical School, 1952.

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Middlesex University School of Medicine, 1940.
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MCGUIRK, DONALD L., 55 Pearl Street, Stoughton.
University of Physicians & Surgeons, Kansas City, 1943.
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Middlesex University School of Medicine, 1941.
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Harvard Medical School, 1951.

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University of Budapest Medical School (Pazmany Peter), 1942.
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University of Rochester School of Medicine, 1951.

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Boston University School of Medicine, 1952.

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Middlesex University School of Medicine, 1945.
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University of California School of Medicine, 1947.

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Harvard Medical School, 1948.

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Harvard Medical School, 1949.

TOMPKINS, WILLIAM D., Boston City Hospital, Boston.
Tufts University School of Medicine, 1951.

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New York State University College of Medicine at New York City, 1951.

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Columbia University College of Physicians & Surgeons, 1946.

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Edinburgh University, 1935.
Sponsor: Dr. Roy J. Ward, 9 Bellevue Street, Worcester.

MASON, EDWARD, 7 Chatham Street, Worcester.
Tufts University School of Medicine, 1952.

MIKOLOSKI, VINCENT S., JR., 101 Chino Avenue, Worcester.
University of Maryland School of Medicine, 1955.

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University of Virginia Department of Medicine, 1943.

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University of Pennsylvania School of Medicine, 1951.

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Tufts University School of Medicine, 1954.

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MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

SPECIMENS FOR LABORATORY EXAMINATION IN FOOD-POISONING OUTBREAKS

From time to time the Diagnostic Laboratory has received samples of food suspected of causing food poisoning, examinations of which have been unwarranted either because of the character of the outbreak involved or because improper or insufficient investigation of the outbreak has been made. A few cases involving a single family rarely constitute a public-health food-poisoning problem. In any case an on-the-spot expert epidemiologic investigation is necessary to ensure the proper specimens for laboratory study. Unsatisfactory specimens not only cause much useless and expensive laboratory work but also make interpretation of the laboratory findings difficult or impossible.

The district health officer, therefore, should be notified before any specimens are sent to the Laboratory. He will decide whether or not the situation warrants a laboratory study and, if so, will direct the proper aseptic collection of food samples in clean containers and determine the specimens needed from the patients and the food handlers. His work will include a complete history of the outbreak, a digest

of which must be passed on to the Laboratory at once.

To avoid wasteful studies that may interfere with more important work, the Laboratory will accept food samples suspected of causing food poisoning only when the outbreak involved is under investigation by a state health officer or epidemiologist, and the investigation indicates that a laboratory study of the food and other specimens will be appropriate and useful.

BOSTON MEDICAL LIBRARY

LAHEY PERIODICAL ROOM

Unveiling of the portrait of Dr. Frank H. Lahey at the dedication of the Lahey Memorial Periodical Room. Standing beside the portrait are Dr. Richard B. Cattell, director of the Lahey Clinic, and Dr. Arthur W. Allen, president of the Library.

CORRESPONDENCE

BENIGN PERIPATESIS

To the Editor: In the August 16 issue of the *Journal* a letter from Dr. Renwick K. Caldwell, Florence, Massachusetts, calls attention to a "Geographic Error" that appeared in the paper by Dr. Bushueff and me, entitled "Disseminated Pulmonary Calcification," in the June 7 issue.

In referring to the case report, "Histoplasmosis in a Life-Long Resident of New England," by French et al. in the August 13, 1953, issue of the *Journal*, we failed to include the state of New Hampshire in addition to the state of Vermont, when we quoted the patient's normal or lifetime residence. Secondly, we omitted the fact that he drove to Boston on four or five occasions, motored to New York City for an overnight trip and, in the winter of 1952, made an automobile trip to the Trudeau Sanatorium, where he was a bed patient for about six weeks, returning to Vermont by car.

Regarding Dr. Caldwell's concern that the patient "not only had been out of Vermont but also had been out of New England," I wish to stress the fact that although the point source of infection with *Histoplasma capsulatum* could be in any geographic location, the *modus operandi* of infection in this case can be regarded as the patient's "employment intermittently for years on a Vermont farm performing the usual farm chores, which included cleaning out of chicken houses," as described by French et al. Moreover, the chance that the patient acquired the infection on a motor trip to Boston and New York City, or on a visit to and hospitalization at the Trudeau Sanatorium, as implied in Dr. Caldwell's letter, is remote indeed. It is generally accepted that exposure to or infection by *H. capsulatum* may result from intimate contact with soil dust contaminated by chicken excreta, to which the patient in question was exposed intermittently for many years on a Vermont farm.

MARK H. JORESS, M.D.
Chief, Thoracic Diseases Section
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Boston

A MATTER OF NOMENCLATURE

To the Editor: The paper by Pollycove, Apt and Colbert, "Pernicious Anemia Due to Dietary Deficiency of Vitamin B_{12}," appearing in the July 26 issue of the *Journal*, raises a question concerning nomenclature of disease. Pernicious anemia was first described a hundred and one years ago by Thomas Addison, though Biermer, in Zurich, described it independently in 1872 and gave the disease its name, calling it "progressive pernicious anemia." Minot is responsible for making it no longer pernicious, and in the thirty years since his discovery of the efficacy of liver extract, a great deal has been learned about its pathophysiology so that we have reached a stage in knowledge where several facts may be stated categorically. The clinical manifestations of this disease are caused by deficiency in tissue stores of vitamin B_{12}, the biologic term for which is cyanocobalamin. This deficiency, in turn, results from the lack of a substance secreted — in man — only in the stomach. This substance, intrinsic factor as described by Castle, is necessary for absorption of vitamin B_{12} from the gut. Thus, pernicious anemia, as originally described by Addison, is a disease originating in the stomach. The clinical manifestations include not only megaloblastic anemia and neurologic lesions but also abnormal cells in the vaginal as well as the gastric mucosa.

However, identical manifestations of vitamin B_{12} deficiency can be found as the result of at least four other totally different mechanisms from intrinsic-factor deficiency (or addisonian pernicious anemia). These are: bacterial interference with absorption or utilization of vitamin B_{12}, such as may occur in the intestinal blind-loop syndrome; parasitic infestation by *Diphyllobothrium latum*, in which this parasite robs the patient of vitamin B_{12} by helping itself to supplies of this vitamin ingested by its host; an inability of the intestine to effect transfer of vitamin B_{12} from its lumen into the body because of intrinsic intestinal disease, such as sprue and some cases of regional enteritis; and, finally, the mechanism described in the paper by Pollycove et al. — failure of the patient to eat foods containing vitamin B_{12}, a mechanism extremely rare in the areas of the world endowed with plentiful food supplies.

Any one of these five different mechanisms producing deficiency of vitamin B_{12} may be the basis for megaloblastic anemia. Since pernicious anemia, as originally described, refers only to the variety caused by failure of the stomach to secrete intrinsic factor, and since it is no longer pernicious at all, perhaps we should abandon this term entirely in favor

of the accurate one of vitamin B_{12} deficiency caused by lack of intrinsic factor. However, man feels more comfortable in continuing traditions, and it is desirable to preserve a historical perspective. Furthermore, we ought to perpetuate the names of illustrious figures in medicine. Thus, if we wish to use the term pernicious anemia it ought to be called addisonian pernicious anemia, but in so doing we must be sure that this means megaloblastic anemia caused by vitamin B_{12} deficiency resulting from defective gastric secretion of Castle's intrinsic factor.

Other manifestations of vitamin B_{12} deficiency, of which the case reported by Pollycove and his associates appears to be one, are not addisonian pernicious anemia as defined above. (It should be mentioned that the authors touch on this point of nomenclature in one paragraph of the discussion.)

In closing I should like to ask our distinguished editor to decide whether addisonian should be spelled with a small or a capital A. (In most of the literature capital A is used.) Personally, I believe it should be small a, since Addison was not Thomas Addisonian.

JAMES A. HALSTED, M.D.
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Note: The editor recommends the use of "Addison's pernicious anemia" because the only definition of "Addisonian," with either capital or lower-case A, that is recognized outside the medical lexicon is "Like or pert. to Joseph Addison or his characteristic writings; hence, clear and urbane in literary style."—ED.

HISTOPLASMOSIS IN PANAMA

To the Editor: The article, "Histoplasmosis: Unraveling the Panamanian puzzle," by J. Winthrop Peabody, Jr., in the August 30 issue of the *Journal* again raises the question of the endemicity of histoplasmosis in Panama. It seems to me that this point has already been amply demonstrated. Grocott's discovery of the disease in a dog, Ajello's isolation of the organism from the soil and Draheim's discovery of the fourth Panamanian case in an infant, as well as 2 cases found in adults in 1952 and 1953, are all indications that the disease is endemic to the area. The previous cases in adults, which Dr. Peabody alluded to in his paper, occurred in a Puerto Rican woman and a soldier whose home was in Hawaii. The woman had lived on the Atlantic side of the Isthmus for a few months before her death; the soldier had been stationed on the Pacific side for sixteen months. It is interesting to note in passing that this third modern case occurred in an Oriental — a Japanese — since Darling's third and last case of 1906 was also an Oriental — the Chinese, Fu Mas.

Dr. Peabody was apparently unaware of the occurrence of clinical cases of nonfatal histoplasmosis. One of these was found in a six-year-old white boy from Pennsylvania who had resided on the Isthmus for less than seven months. He was hospitalized for investigation because of a peculiar shadow in the right-lung field found on an x-ray film taken during a routine physical examination. Tuberculin tests were negative, as well as a long series of attempts to cultivate tubercle bacilli from the sputum and gastric aspirations. The x-ray shadow in the chest began to regress spontaneously after two weeks in the hospital; and the histoplasmin skin test done at this time was strongly positive. Eventually, the chest films appeared normal. This case occurred during 1952 and was signed out as "histoplasmosis" on the Gorgas Hospital chart.

The hiatus of nearly fifty years between the original discovery of histoplasmosis and the newest series of cases is extremely interesting. Panama is an area where every pathologist and practicing physician is acutely aware of the existence of histoplasmosis. The percentage of autopsy examination done at Gorgas Hospital is extremely high, and any well defined case of histoplasmosis would probably be quickly recognized. Yet no cases were recognized between 1906 and 1951. This suggests that there may have been some climatic condition, or change in the relation of persons to the soil during the period since 1951 that again permits serious infections with the fungus. Perhaps epidemiologic studies on the Isthmus, in the land where histoplasmosis was first recognized, might shed light on the perplexing problem of the manner in which this disease causes infections in man.

I must object to the term "naïveté" as applied to Dr. Darling's proposal that histoplasmosis may have been wiped out of the area by the rapidly improving sanitary conditions in the Canal Zone. Darling was a keen and astute observer, and anything but naïve. He had more than a little reason for adopting this belief. He had discovered his 3 cases of histoplasmosis in an autopsy series of about 500 cases. He failed to find any evidence of histoplasmosis in a series of over 1500 autopsies done between 1906 and 1909, during the interval between the discovery of his third and last case and his final paper on the subject. He was unaware that the organism *Histoplasma capsulatum* was a fungus rather than a protozoan, until the studies of Da Rocha Lima showed this to be true in 1913. Consequently, assuming that the organism was a protozoan and recognizing the fact that cases had disappeared, what could seem more logical than that the efforts to sanitate the Canal Zone were responsible? It should never be forgotten that it was not until 1925 — the year of Dr. Darling's untimely death — that another case of histoplasmosis was recognized in Minnesota. This was the first case to be reported from anywhere in the world since Darling's cases discovered in Panama.

MICHAEL J. TAKOS, M.D.
Hialeah, Florida

WORTHY OF A BETTER HIRE

To the Editor: In Dr. Jewett's report from the Committee on Maternal Welfare of afibrinogenemia after rupture of the uterus in the August 23 issue of the *Journal* I detect a critical attitude toward the laboratory technician who reported a dissolving clot three hours late.

It is not at all impossible that this technician was involved in half a dozen other procedures simultaneously on as many patients so that the one under discussion did not have his undivided attention.

In Massachusetts and Northern New England, where technical staffs are overworked and grossly underpaid, perhaps New England medicine in general would do well to survey an unhealthy situation that is growing worse. In no other medical field has neglect of a group proved so critical.

The laboratory and x-ray technical fields offering such low economic returns can no longer attract good material. Responsible work deserves an adequate living wage.

RICHARD B. EARLE, R.T.
Center Conway, New Hampshire

PYELITIS–PYELONEPHRITIS

To the Editor: Regarding Dr. Harry A. Derow's Medical Progress report, "Management of Pyelonephritis," in the August 9 and 23 issues of the *Journal*, I should like to offer some possible anatomic physiologic and etiologic factors concerning pyelitis-pyelonephritis as a complication of pregnancy.

To the best of my recollection, the term "pyelitis" was not mentioned at all, as if this and "pyelonephritis" were synonymous. Histologically and pathologically there is a distinct difference.

Although the general atony associated with pregnancy may produce a certain degree of hydroureter, that on the right side (where infections are more prevalent) may be aggravated by the following factors:

The right ureter is in more direct contact with the underlying pelvic brim, unlike the contralateral ureter, where the iliac vessels are to some extent interposed.

The pregnant uterus, as it enlarges into the pelvis, tends to lie toward the right side and is somewhat rotated to the right.

It seems logical to assume that — on the right side, anyway — obstruction (relative or partial) by the gravid uterus would be more prevalent, causing (a greater degree of) hydroureter due to "kinking" at the pelvic brim.

MICHAEL J. O'KANE, M.D.

Metuchen, New Jersey

REGARDING PERIODIC REGISTRATION

To the Editor: I was very much interested in the editorial in the September 6 issue of the *Journal* regarding periodic registration of physicians. I certainly favor the periodic registration of physicians in Massachusetts. Dentists are required to do so, as well as barbers and hair dressers. Why should not physicians be required to register and pay the small annual fee?

I think this is a step forward — and a necessary one if the number of physicians practicing medicine in this state is to be known. The fee required for such registration is immaterial.

GERARDO M. BALBONI, M.D.

Boston

BOOK REVIEWS

Die Occipito-Cervical-Gegend: Eine diagnostisch-pathogenetische Studie. By Priv.-Doz. Dr. J. E. W. Brocher, Genf. 4°, cloth, 145 pp., with 91 illustrations and 1 table. Stuttgart: Georg Thieme, 1955. $11.40. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

As the author states in his foreword, much has been published about the pathology of the vertebral column since Schmorl did his classic work, but few books are available concerning the occipitocervical region in particular.

The anatomy and embryology of the craniovertebral junction are briefly discussed, and the particular function and methods of x-ray examination are described. The author surveys the current knowledge of diagnosis and pathogenesis, with frequent references to both the English-language and European literature. Many illustrations with clinical data complete the systematic review. The positive x-ray reproductions are unfortunately not up to the usual European standard. The important contribution of the book is the 60-page section devoted to malformations of the occipitocervical region.

JOACHIM BURHENNE, M.D.

Receptors and Sensory Perception: A discussion of aims, means, and results of electrophysiological research into the process of reception. By Ragnar Granit. 8°, cloth, 369 pp., with 145 illustrations. New Haven: Yale University Press, 1955. $5.00.

This book represents the material given at the Silliman lectures at Yale University School of Medicine in 1954. The author is complimented for his impeccable English and the easy style of his paragraphing and sentence structure, since a professor from Stockholm, Sweden, would not be expected, in writing in a foreign language, to avoid a number of awkward usages and lengthy sentences. It is refreshing to find the text so easy to read. The only drawback is his continual arrangement of dates and names in parentheses in his sentences to cover the facts that he utilizes from the extensive world literature. This makes it a little more difficult to grasp as one reads paragraph after paragraph.

The book is profusely illustrated with original figures of the author's research and from his published material, and also from a large number of published papers by his colleagues. The bibliography at the end of the book is as complete a one on the subject of the neurophysiology of receptors in animals and human beings as I have ever seen.

Granit introduces the subject by a brief and interesting historical background of the theoretical concepts of how sensory organs in living creatures function. He then promises to correlate these ideas of the early masters in physiology with recent experimental neurophysiology using modern technics of high-fidelity cathode-ray oscillographic recording. This plan of his book makes it a fascinating text in which to delve but makes it exceedingly difficult to read continuously.

One of Granit's theses is that the most efficient type of sense organ would be one that had some type of spontaneous rhythmical electric discharge in the absence of any direct stimulation. This spontaneous discharge could, therefore, under the influence of stimulation, be increased in its amplitude, decreased in its amplitude or altered in its frequency characteristics. This would be a distinct advantage over a sense organ that was totally inactive and then became active only under stimulation, thereby giving only one parameter to indicate its response.

The first 100 pages give example after example of how the sense organs under study, including the eye, the ear, the vestibular apparatus and the skin and muscle sense organs, in their responses give strong evidence that they have either a purely spontaneous rhythm of their own or one that is established by the existence of spontaneous feedback in neural circuits. The author goes into more detail about the visual apparatus than any other because it is his primary interest. His greatest contributions have been in the field of the electroretinogram in animals and in man. In fact his chapter on the theories of vision and the experimental work in the last ten years connected with the retinal responses and their transmission through the lower centers to the cerebral cortex is the most important part of the book. He shows clearly the need in the nervous system of economy of transmission fibers when a sense organ as complicated as the eye is involved. Twenty retinal elements, for example, can be discharged through one nerve fiber, effecting considerable economy. He also brings in interesting evidence that responses from both the rods and cones (scotopic and photopic) can be received by the brain through the same neural networks.

An interesting discussion in the middle of the book reviews the extensive literature, the conflicting theories and the interpretation of different experimental results concerning the biochemistry of retinal pigments. In places the author agrees thoroughly with the meticulous, careful work of Wald at Harvard; in others, he disagrees in no uncertain terms with some of Wald's interpretations. Considerable argument is covered in this section concerning dominators and modulators in the retinal physiology. The dominators, which cover broad-band color frequencies, can exist according to Granit in all creatures that he has studied along with the modulators, which cover the narrow bands and have individual chemical pigments. Some of the numbers he gives are of interest to the clinician who would take up this book. For instance, he states that one rod in an animal's eye would have in its structure between 12,000,000 and 18,000,000 molecules of rhodopsin. Calculations would show that a modern intensity of five-second flash of light would transform only 1200 of these in the formation of a signal that could go through the nervous system.

The detailed description of the electroretinogram, or ERG, covers a tremendous amount of experimental work in all levels of animal development showing that this electric event can be altered by the intensity of light, color of light, the rate of on-and-off response, flicker and whether the eye is dark-adapted or light-adapted. The author thinks that there is evidence of coding in the neurologic conduction of the visual impulses through the brain so that different wave lengths or colors can produce different spike rates. These differences, he points out, however, are not nearly so specific as in the auditory nerve, where the different wave lengths of sound are reported by specific code differences in the nerves and in different areas in the auditory cortex where these primary responses project.

Granit emphasizes the importance of pioneers like Adrian in showing in the animal double-sensory-projection fields, which have been mapped out in the human by Penfield as an accessory sensory area.

The most interesting description of the little understood gamma fibers that run to muscle spindles and cutaneous skin endings is covered in the latter part of the book. In the final chapter, discussing the ultimate meaning of sensory stimulation to the awake and functioning animal, the author points out the complexity of the central nervous system even in lower animals when he mentions that 1 neuron running into the thalamus from a sensory organ may influence or activate as many as 5000 individual neurons in the area. Here, he covers briefly his concept of what a feed-back mechanism can do even when it is a simple one connected with a stretch reflex in increasing efficiency, sensitivity and variability in the type of responses that the living creature depends on.

As stated above, one doubts whether many clinicians would pick this book up and read it through, for the amount of factual material is so intensely concentrated that retention of information by direct reading would be difficult. However, many clinicians in all kinds of fields will probably like to read parts of this book, again and again, over many months and years, because of the application of so much of this material to better understanding of the functions of the brain and mind in man. It is obvious, too, that the greatest interest is in the highest-developed sensory system of man — namely, the visual apparatus from retina through mid-brain and occipital cortex.

ROBERT S. SCHWAB, M.D.

Management of Addictions. Edited by Edward Podolsky, M.D. 8°, cloth, 413 pp., with illustrations. New York: Philosophical Library, 1955. $7.50.

This heterogenous collection of thirty-five unrelated papers on various aspects of alcoholism and drug addiction, previously published separately in some nineteen scientific journals, had the bad luck to be seriously out-dated before publication: all the papers were written before the advent of the new tranquilizing drugs, such as chlorpromazine, reserpine and meprobamate, which now seem destined to be very important in the management of addictions. The choice of papers by the editor is puzzling and very uneven: some of them such as Lolli's chapter "On Therapeutic Success in Alcoholism" and the report of the careful evaluation of Antabuse by Bowman and his associates are well worth reprinting; many of the other papers could have been charitably left in their original tombs. There are some notable omissions such as the publications from the Alcoholic Unit of the Medical College of Virginia, which is not represented at all. The book is poorly printed and has inexcusable typographic errors; it is probably only of reference and historical interest and of no particular value to medical students, general practitioners or specialists.

ROBERT FLEMING, M.D.

Urology. By B. G. Clarke, M.D.; and Louis R. M. Del Guercio, M.D. 8°, cloth, 245 pp., with 162 illustrations and a frontispiece. New York: The Blakiston Division, McGraw-Hill Book Company, Incorporated, 1956. $6.50.

The preparation of this book was prompted by the popular demand of the senior author's students. Its purpose is clearly stated by the authors to be that of providing the essentials of urology desirable in undergraduate study, and this end has been well accomplished. Conciseness, brevity of script, graphic illustrations and a well organized bibliography for each topic discussed furnish basic information, a stimulus for further study and an easy guide for further investigation of special interest in any aspect of urology and related subjects.

The plan of the book is well conceived in logical sequence and efficiently expedited by simple statement of well proved fact. Confusion is avoided by omission of unsettled controversy. The sound principles of visual education are utilized effectively and extensively to help the student, resident and practitioner in their understanding of urologic problems. Physical diagnosis, physiology, roentgenology, pathology and surgical and medical management are appropriately presented in text and illustrations accompanied by specific references constituting an up-to-date bibliography. It is anticipated that this book will be useful to students, physicians, surgeons and urologists. The authors are congratulated upon their accomplishment and encouraged in their dedication to medical education.

J. HARTWELL HARRISON, M.D.

Complications of Regional Anesthesia: Etiology, signs and symptoms, treatment. By Daniel C. Moore, M.D. 4°, cloth, 291 pp., with 51 illustrations and 25 tables. Springfield, Illinois: Charles C Thomas, 1955. $10.50.

This presentation of the various complications related to drugs for local anesthesia and technics of regional anesthesia is concise and extremely well organized. The book is divided into three parts: the first discusses the complications of local infiltration and peripheral-nerve-block anesthesia, including toxic reactions to the anesthetic drugs and trauma associated with the technic; the second considers the complications of spinal and epidural block; and the third mentions incidental complications.

The discussion of the complications related to spinal anesthesia, regional technics and local toxic drug reactions is based on a review of the literature as well as the author's extensive experience. He has avoided controversial issues. However, he emphasizes the importance of meticulous care in preparation of the drugs and equipment, and explains in detail how to avoid complications. The etiology, signs and symptoms, prophylaxis and treatment of each complication are discussed. The tables on incidence of complications with various technics and drugs are comprehensive and serve as excellent reference material.

This textbook is recommended to any physician who uses regional anesthesia.

BENJAMIN ETSTEN, M.D.

The Treatment of Renal Failure: Therapeutic principles in the management of acute and chronic uremia. By John P. Merrill, M.D. 8°, cloth, 238 pp., with 31 illustrations and 16 tables. New York: Grune and Stratton, 1955. $6.75.

This book organizes and summarizes a wealth of important material about renal disease and renal physiology. It presents a practical approach to the treatment of renal failure. It includes the author's philosophy of renal physiology, and through these concepts, based on a wide experience in this field, the successive chapters evolve a clear understanding of the disease and its clinical treatment. This book is equally amenable to the needs of the student and the expert in renal disease. The modest presentation of such a complicated subject reflects the author's background and understanding of the renal mechanism. Considering the complexity of the subject, his style makes the book a genuine pleasure to read. The book lends itself to reference and offers an excellent bibliography of the field. This book should be read by all interested in general medicine, for the problem of renal failure, either acute or chronic, is a constant problem in the study of disease. It emphasizes the importance of prompt recognition and accurate treatment of reversible disturbances that are essential in modern medical practice.

F. CORBIN MOISTER, M.D.

The Clinical Approach in Medical Practice. By G. E. Beaumont, M.A., D.M., F.R.C.P., D.P.H. 8°, cloth, 469 pp., with 74 illustrations. London: J. & A. Churchill, Limited, 1956. $9.00. (Distributed in the United States by Little, Brown and Company, Boston.)

Dr. Beaumont, in this scholarly and entertaining book, has contributed immeasurably to the technic of medical education. In a series of illustrative case histories, written with all the skill and suspense of a master of detective fic-

tion, he has combined the finest points of the neglected art of clinical observation with the most modern methods of medical science in tracking down the criminals of disease.

The first portion of the book is devoted to a series of narrative accounts of the author's experience as a consultant in arriving at a diagnosis, on the basis of many and varied clues in 36 individual cases, each one selected as illustrating an important disease or significant symptom. The accounts are enlivened by many personal anecdotes with a direct bearing on the case at hand. The author-detective is usually successful in solving the mystery, but he is always willing to admit his failures and to profit thereby.

The central portion of the book is composed of descriptions of the emotional reactions of patients to the discovery that they are afflicted with tuberculosis. Here, the author draws upon his long experience as a phthisiologist and delves, perhaps a little superficially, into the psychologic lives of his patients. Included in this section are some philosophical reflections upon the wisdom of prolonging the lives of patients with severe congestive heart failure, with some examples illustrating both sides of the argument.

The final section of the book consists of a series of clinical teaching exercises based on case demonstrations enlivened by a bright exchange of questions and answers between teacher and students. The importance of physical signs and symptoms is emphasized throughout, but the very latest diagnostic procedures are described and their place in differential diagnosis clearly defined. Included in each exercise is an erudite résumé of the historical facts pertinent to the case under discussion, which lends a rich academic flavor to the art of pedagogy too often lost sight of in the present-day emphasis on the purely practical.

Every practitioner of medicine will recognize some of his own problems in these pages and will derive both knowledge and satisfaction as the solution unfolds. Medical students, general practitioners and specialists alike will find this book a most enjoyable way of broadening their professional education.

KENDALL EMERSON, JR., M.D.

Disorders of Character: Persistent enuresis, juvenile delinquency, and psychopathic personality. By Joseph J. Michaels, M.D. 8°, cloth, 148 pp., with 11 tables. Springfield, Illinois: Charles C Thomas, 1955. $4.75.

This volume represents twenty-five years of careful thought and work devoted to a single subject, a subject that every physician realizes as one of the most difficult and challenging in medicine. Dr. Michaels is trained as a psychiatrist, but he writes like a physician and a scientist, and brings to bear the powerful tools of objectivity and observation when he deals with his materials. Now that the neuroses and psychoses have become more definitely outlined, Dr. Michaels proceeds somewhat as an explorer might into the vast *terra incognita* of disorders of character, and in doing this he carries few instruments, but he has basic ideas for orientation that he emphasizes frequently and never lets out of sight. They are the basic symptoms of persistent enuresis, juvenile delinquency and so-called psychopathic personality. This is the triad that keeps the vast system of municipal, state and federal courts and prisons busy and is the reason for the existence of the present probation and penal correction systems. Certainly, enuresis is a physiologic problem. It might be described as failure or inability to control the emptying of the urinary bladder. But with great understanding and enormous stock taking and itemization, Dr. Michaels correlates the symptoms of persistent enuresis with other neurotic and character disturbances in such a way that his work and his interpretations may now be considered paramount and remarkably well integrated into the over-all picture of medicine and psychiatry as it stands today. Many years ago he discovered that a high incidence and long persistence of enuresis are found among those with the character disturbances called psychiatric behavior problems, juvenile delinquency and psychopathic personality. He has extended, amplified and tested this observation in many fields: in his private practice, as a psychoanalyst, during his military service as an Army psychiatrist, and as a lecturer and instructor in the Department of Psychiatry at Harvard Medical School, the Boston Psycho-Analytic Society and Institute, the Beth Israel Hospital, Boston, and many other places. Some of the material in this book, incidentally, was given, under the directorship of Anna Freud, in the form of lectures before the Hampstead Clinic in London, where they were warmly received.

And it is high time that some authority investigated this problem to the fullest extent of present-day facilities, because persistent enuresis plagues parents and pediatricians and because, wherever human beings live—whether in family or institutional circumstances — the persistent bed wetter has always been one of the permanent problems of mankind. Mortification, embarrassment, annoyance and inconvenience are the slightest consequences of this malady. Dr. Michaels takes a broad view. His interpretation is in line with the "unified field policy" that relates all human behavior, both individual and group, into a comprehensible and forward-looking theory. Experienced pediatric clinicians have always sensed in persistent enuresis a problem different from and more serious than the other symptoms of childhood, and psychiatrists have realized for a long time that the disorder might be compared to any neurotic manifestation arising from the same etiologic level as anxiety symptoms. Dr. Michaels, as a psychoanalyst, proposes in this summation of twenty-five years of research that there may be a psychosomatic disposition specific to the delinquent type of personality with a history of persistent enuresis. He stresses the complex experiential factors that emerge in all behavior and gives due credit to psychoanalytic interpretations of persistent enuresis, juvenile delinquency and psychopathic personality. Although present knowledge of these three conditions is still very much in the research stage, the feeling of the book is clinical, and there is an undertone of hope in the dynamic conclusions drawn by the author.

The book is compact and well written and ranges from careful statistical studies to interpretations that embody various conceptions of theoretical consequence. All in all, it stands as a milestone in its development of a comprehensive (biopsychosocial) view of persistent enuresis in its relation to delinquency and psychopathy. It will be valuable to student, physician, specialist and intelligent readers for a long time to come. The publishers have done their customary excellent printing job with this book.

MERRILL MOORE, M.D.

Biochemistry and the Central Nervous System. By Henry McIlwain, Ph.D., D.Sc. 8°, cloth, 272 pp., with 43 illustrations and 33 tables. Boston: Little, Brown and Company, 1955. $9.50.

In this book Professor McIlwain has accomplished the difficult task of dealing with most of the main aspects of the biochemistry of the central nervous system and condensing them into one concise volume. He begins with a discussion of the metabolism of the brain *in situ*, and, after a short chapter dealing with the chemical composition of the brain, proceeds to deal with the metabolism of the brain in vitro. This is discussed quite fully from the points of view of both the tissue preparations that have been used and the metabolic systems that have been studied. A separate chapter deals with the importance of the vitamins to the nervous system. The author then gives a compact review of the knowledge of the structure of the brain from the chemical and histologic points of view, and discusses the biochemical development of the brain in the growing organism. The final chapters deal with the pharmacologic aspects of brain biochemistry, regarding both the occurrence and actions of intrinsic neurohormones and the effects of administered drugs.

Since Professor McIlwain's main interest and work are concerned with the dynamic aspects of brain biochemistry, his book is naturally biased in that direction. Nevertheless, he has covered the other aspects quite well, and, although the bibliography was not intended to be exhaustively complete, all the important literature is included and unusually

well annotated in the text. It is unfortunate that the large amount of subject matter covered in this book necessitates a rather didactic treatment, to the detriment of a more critical evaluation of the work discussed.

F. N. LeBaron, Ph.D.

Chemistry and Human Health. By Burnham S. Walker, M.D., Ph.D.; and M. Kolaya Nicholas, R.N., M.A. 8°, cloth, 445 pp., with 10 illustrations, 47 tables and 243 formulas. New York: The Blakiston Division, McGraw-Hill Book Company, Incorporated, 1956. $5.75.

In general the authors have done remarkably well in compressing the outlines of inorganic, physical and organic chemistry and biochemistry into one treatment. The student who uses the book will get a glimpse of these important fields, but with slight risk of believing, when it is all over, that modern chemistry is indeed a simple matter. The introductory definitions are illustrated with pithy examples, which are suitably designed to arouse the curiosity and interest of persons not previously oriented to science.

The treatment of electrolytes and acids and bases is modern in all respects, Brønsted terms being used for acids and bases. The clarity and simplicity of the presentation is a tribute to the authors. Similarly, the treatment of amino acids as dipolar ions is simple but accurate.

Protein metabolism is presented almost in outline form; most of the important aspects of the problem are mentioned. Despite this, there are occasional departures from the basic facts to more esoteric facets of the subject — for example, the details of histidine metabolism to N-formylglutamine.

This volume is highly recommended, however, to nursing schools and to students desiring a chemical orientation as an ancillary tool in scientific growth.

James L. Tullis, M.D.

Neurochemistry: The chemical dynamics of brain and nerve. Edited by K. A. C. Elliott, M.Sc., Ph.D., Sc.D.; Irvine H. Page, M.D.; and J. H. Quastel, D.Sc., Ph.D., A.R.C.S., F.R.I.C., F.R.S.C., F.R.S., F.C.I.C. 8°, cloth, 900 pp., with illustrations and tables. Springfield, Illinois: Charles C Thomas, 1955. $19.50.

This is an ambitious compendium of thirty-two articles contributed by a galaxy of distinguished investigators with the object of furthering "the understanding of the phenomena underlying the behavior of nerve, brain and mind, and the maladies to which they are subject." The critic is disarmed not only by the respect that such a goal evokes, but also by the oft-reiterated implication in most of the chapters that the presentations in each field are neither comprehensive nor correlatable. If allowance is also made for the fact that the works cited in the majority of the articles were published before 1951 (with a few references to publications in 1952), the omissions in the chapter, "Chemical Constituents of Brain and Nerve," by R. J. Rossiter, especially in the fields of water-soluble glycolipids, and the need for re-evaluation of analytical values for tissues owing to recently introduced analytical and chromatographic methods become excusable. If many of the authors had themselves taken note of the caution expressed in the excellent chapter, "Biochemistry of Brain during Early Development," by W. M. Sperry, regarding extraction, isolation and analytical procedures used by earlier workers, much of the emphasis placed on analytical values for brain and nerve (especially with reference to lipids, ribonucleic acid and desoxyribose nucleic acid), and the conclusions drawn therefrom would have been revised even in 1952.

In a book of this size and scope a certain unevenness in the quality of various chapters and considerable overlapping and repetition are unavoidable. In the first chapter, by Irvine H. Page, a glowing tribute is paid to Thudichum, emphasizing the meticulous and painstaking work of the founder of neurochemistry. The substance of this chapter unconsciously stands in eloquent and somewhat reproachful contrast to the last chapter of the book ("Thermodynamics of the Message," by Norbert Wiener), where unrestrained speculations based on dubious analogies would confuse the reader unfamiliar with cybernetics. However, besides the chapter by Sperry already mentioned, some chapters like "Metabolism of Glutamic Acid and Glutamine," by Heinrich Waelsch, "Noradrenaline in Adrenergic Nerves," by U. S. von Euler, "Metabolism and Function in the Nervous System," by R. W. Gerard, "The Neurotropic Drugs," by J. E. P. Toman, "Biochemistry of Demyelination," by R. J. Rossiter, and "Structure, Chemistry and Pathology of the Central Nervous System of Arthropods," by A. Glenn Richards, are outstanding in the material selected for discussion, and the authoritative manner in which the data available in each field are correlated. This reviewer considers it unfortunate that L. S. Penrose chose to deal with "Inborn Errors of Metabolism in Relation to Mental Pathology" so briefly (pp. 807-818) since this topic would have provided an excellent ground for correlation of the knowledge of the normal chemical constituents and metabolism of brain with some metabolic abnormalities that can have striking outcomes in brain structure and function. In this connection, it should be pointed out that much of the information available during the past three years on the chemical nature of the storage substances in the lipoidoses is missing from this book, with the result that these sections of the discussion tend to give an erroneous view to the average reader seeking specific information or orientation.

Notwithstanding these shortcomings the editors of the book should be thanked for the enormous amount of effort that such a compendium entails, and the valuable service they have rendered those interested in "neurochemistry." To the expert, the book provides a handy source of references in each field, and those whose interest has more recently been stimulated to explore the structure and function of nervous tissue at a molecular level will be rewarded by a panoramic and instructive survey of previous effort.

L. Lahut Uzman, M.D.

The Practice of Medicine. Edited by John S. Richardson, M.V.O., M.A., M.D. (Cantab.), F.R.C.P. 8°, cloth, 1076 pp., with 86 illustrations and 10 tables. London: J. and A. Churchill, Limited, 1956. $8.50. (Distributed in the United States by Little, Brown and Company, Boston.)

This book by John S. Richardson of St. Thomas's Hospital, London, and a distinguished group of British collaborators is a complete and up-to-date treatise on the practice of medicine as seen by eminent English physicians. It has a unique first chapter on the nature of disease that is a departure from the usual medical textbook. This consists of a semihistorical philosophical treatise on the general principles and beliefs concerning disease. It makes very interesting reading and certainly gives a background for what is to follow in subsequent chapters.

The second chapter discusses various antibacterial drugs. Many would take issue with the opinion of Fletcher, the author of this chapter, that of the sulfonamides it is only necessary to consider sulfamezathine, succinylsulfathiazole and sodium sulfacetimide. Nothing is said about the triple sulfonamides, sulfadiazine and sulfisoxazole, which are in such widespread use in this country. Certainly, a much more thorough discussion of the antibacterial drugs would have been better in this chapter.

The next 150 pages deal with diseases of the respiratory system, which is covered adequately and in a readable manner. The radiographic plates describing various lesions in tuberculosis are particularly good reproductions. One is impressed by the difference in the English approach to the treatment of tuberculosis, especially mechanical procedures. Apparently, the author still considers artificial pneumothorax and pneumoperitoneum a widespread form of treatment in Great Britain. He regards pulmonary resection as not having a thoroughly established role in treatment.

The section dealing with cardiovascular disease is complete, and again one is impressed by the excellent x-ray reproductions. The section on hypertension is exceptionally well done. A somewhat disturbing feature in certain sections is the frequent use of grains to describe dosage of medicine. This practice has practically disappeared in the United States — and justifiably so. However, in England the grain system is still widely employed.

The book throughout makes interesting reading and certainly presents the English view of medicine in a very satisfactory manner. There are many points of difference between the practice of medicine there and that in this country, and as one reads, the genuine impression is formed that many of the procedures that are quite new in this country but are a good, accepted practice are not in use there or are considered by British colleagues as being of more experimental nature. One is impressed by the completeness of the book, and undoubtedly it serves very well the purpose for which it was written. There is a useful appendix, which gives instructions for low-sodium diets, low-residue diets, high-protein and low-sodium diets and other special dietary measures. A table of normal laboratory values is also very complete and useful.

DALE G. FRIEND, M.D.

Treatment of Migraine. By John R. Graham, M.D. 12°, cloth, 149 pp., with 8 illustrations. Boston: Little, Brown and Company, 1956. $4.00.

Dr. Graham has admirably put forth in this small monograph the essentials of the diagnosis, treatment and prevention of migraine headaches. Particularly emphasized is the importance in management of a thorough knowledge of the patient as a whole, including an appreciation of the type of personality and the various factors, social, economic and otherwise, that beset him. The need of a proper patient-doctor relation is stressed.

A fairly complete review of the various drugs, past and present, used in the treatment of migraine, is briefly, but critically, presented, and the practicing physician is given specific details regarding the use of these agents and the results to be expected from them. A practical plan of management is outlined for almost every potential situation that may arise in the patient with migraine.

Throughout the volume brief case reports illustrate points of importance.

MARK AISNER, M.D.

Pulmonary Carcinoma: Pathogenesis, diagnosis, and treatment. Edited by Edgar Mayer, M.D.; and Herbert C. Maier, M.D. 8°, cloth, 540 pp., with 182 illustrations and 4 colored plates. New York: New York University Press, 1956. $15.00. (Distributed by the J. B. Lippincott Company, Philadelphia and New York City.)

This volume of more than 500 pages is a series of articles by some eighteen distinguished contributors covering all aspects of the subject. Cancer research, the biology of cancer, use of radioisotopes and the psychologic aspects of the disease are discussed along with some of the more conventional approaches to the problem such as its pathological and clinical aspects. Of particular interest is an appendix of unusual case presentations at the back of the book, each with a brief history, roentgenograms and the lesson to be learned.

Altogether, this is an excellent book. It is thorough and clear and presented in a reasonable manner. The bibliography is adequate without any attempt to be exhaustive. Varying points of view are presented without prejudice. For either reference or informative reading both practitioners and students will find this a valuable work.

LAMAR SOUTTER, M.D.

Electrodiagnosis and Electromyography: Some clinical applications of electroneurophysiology. Edited by Sidney Licht, M.D. 8°, cloth, 272 pp., with 90 illustrations and 1 table. New Haven: Elizabeth Licht, 1956. $10.00.

Electric currents for diagnostic purposes are not new, but their clinical use has only recently been centered in the field of physical medicine and this is the first textbook by a physiatrist on this subject. Electromyography is a more recent electrodiagnostic development useful to all interested in neuromuscular function. A comprehensive history of the development of these technics is found in the first chapter of this book.

Two chapters dealing with fundamental concepts follow. There is an adequate discussion of the physics of the testing currents and the apparatus available. The chapter on electrophysiology is particularly detailed and presented on the level of the laboratory physiologist.

The chapters on clinical testing are not unlike similar chapters in available textbooks, with the exception of the sections on chronaxy and strength-duration curves, which are unusually detailed, with consideration of fundamental electrophysiology.

Other chapters cover electromyography, primarily on a clinical level, as well as measurement of electric skin resistance. The appendix includes two short sections on electroencephalography and electroretinography.

One can wholeheartedly recommend this textbook for the reference library of physiatrists, neurologists and the researcher in neurophysiology. It is perhaps too profound for practicing physicians or surgeons only occasionally dealing with lower-motor-neuron pathology. Editorial comment for the benefit of such readers would have been helpful in clarification of the chapters dealing with basic laboratory physiology. More illustrative clinical material would also have added to its value.

ARTHUR L. WATKINS, M.D.

Fractures of the Facial Skeleton. By N. L. Rowe, F.D.S.R.C.S. (Eng.), L.R.C.P. (Lond.), M.R.C.S. (Eng.), L.M.S.S.A. (Lond.), H.D.D.R.C.S. (Edin.); and H. C. Killey, F.D.S.R.C.S. (Eng.), L.R.C.P. (Lond.), M.R.C.S. (Eng.), L.M.S.S.A. (Lond.), H.D.D.R.C.S. (Edin.). With a foreword by Sir Reginald Watson-Jones, B.Sc., M.Ch. Orth., F.R.C.S. 4°, cloth, 923 pp., with 1231 illustrations. Baltimore: The Williams and Wilkins Company, 1955. $22.00.

This comprehensive treatise on facial injuries was written by two experienced surgeons and an impressive list of contributors.

As the authors state, the anatomic complexity of the head and neck enlists the interest of specialists in many overlapping fields. The book, therefore, has been written to appeal not only to the maxillofacial surgeon but also to the plastic surgeon, the neurosurgeon, the ophthalmic surgeon, the orthopedic surgeon, the otolaryngologist and the dental surgeon.

The introduction covers a brief historical review of the progress of maxillofacial surgery in wartime, and presents a detailed statistical outline of the various causes and types of fractures of the facial bones. The main section is divided into three parts. The first, devoted mainly to the mandible, deals with surgical anatomy, general considerations and classification of mandibular fractures, examination, technics of various methods of immobilization and the treatment of anatomically specific fractures, abundantly illustrated with photographs and diagrams. The second part, which covers fractures of the middle third of the facial skeleton, discusses surgical anatomy, preliminary care and general principles of treatment, and the specific treatment of various fractures of the nose, sinuses, zygomatic arch and maxilla. Complications arising in the treatment of fractures in these regions are well handled. The third part covers miscellaneous subjects related to maxillofacial injuries, including gunshot

wounds of the face and jaws, anesthesia, radiology, bone-grafting technic and scalp and head injuries. There is an interesting chapter on the historical background of the treatment of maxillofacial injuries. The book has a long and well chosen bibliography.

It is evident that the authors have spent considerable effort in this very worth-while text. They will be gratified by its enthusiastic acceptance by surgeons everywhere.

V. H. KAZANJIAN, M.D.

The Recovery Room: Immediate postoperative management. By Max S. Sadove, M.D.; and James H. Cross, M.D. 8°, cloth, 597 pp., with illustrations. Philadelphia: W. B. Saunders Company, 1956. $12.00.

The title of this book is somewhat misleading, since the common interpretation of "the recovery room" means a space set apart for immediate postoperative care. This has been well recognized throughout the country for some years as an important adjunct to the proper management of patients. This room is usually staffed with experienced personnel, and located close to the operating pavilion so that the anesthesia department and surgical staff are easily accessible. The usual plan, under these circumstances, is to return the patient to his room or ward as soon as consciousness is thoroughly established or his condition requires no further attention from the standpoint of bronchial aspirations, control of hemorrhage, shock and so forth.

In this volume, there is a much broader interpretation of the problem. That is, all seriously ill patients are cared for in a special area for a period of perhaps twenty-four hours or longer. The authors propose that this ward be set up near the central supply room, and staffed with well trained personnel, around the clock. Every large general hospital could well take advantage of such a ward. In some institutions, probably the emergency ward, so-called, now takes over a part of this responsibility.

Interestingly enough, great detail is given by twenty-four authorities in their various special fields. This includes not only all the surgical specialties but also anesthesia, blood bank, medical consultants and specially trained nurses for the seriously sick. This ideal arrangement is certainly one that should be carefully considered in all hospitals of more than 100 beds.

Various outlines of different-sized units are described, and the administrative phase of the problem discussed.

The detailed postoperative care in relation to different types of surgery is impressive. One would suppose that the chief of each special service might review this book, particularly the section pertaining to his own specialty, and add or delete any features that he considered not in accord with his own experience or desire.

Having gone over this book from beginning to end, I am personally impressed with the soundness of most of the routine measures advocated. Certainly, every hospital should have this volume available for its house staff. If the directors of various units wish to leave the house staff alone with the suggestions offered, they would in many cases, improve patient care. Even for institutions where much thought has been given to this acute phase of surgery, many valuable suggestions can be found in this volume.

ARTHUR W. ALLEN, M.D.

Obstetrical Anesthesia: Its principles and practice. By Bert B. Hershenson, M.D. With a foreword by Frederick C. Irving, M.D. 8°, cloth, 403 pp., with 50 illustrations and 17 tables. Springfield, Illinois: Charles C Thomas, 1955. $9.50.

This carefully written, dogmatic, general anesthesiologic textbook with special reference to obstetric anesthesia, is basic in character and designed to teach the novice in the art of anesthesia. It outlines and directs the clinical application of these physiologic and pharmacologic principles to the parturient patient. The frequent use of outlines, tables and sequentially outlined instructions provides easy reference. The author apparently has an intimate familiarity with current medical literature, evidence for which is sprinkled throughout the book. It is interesting to note in this regard that a page is assigned to electroencephalography. The author tends to present one point of view, and permits very little contradiction to creep in, which is an advantage to the tyro.

Of particular note is the chapter on infant resuscitation, which presents in complete form the latest opinions. Dr. Hershenson's treatment of this subject is detailed and follows a logical course of diagnosis, pathology and therapy. He includes his own published work on premedication, which has not received popular acclaim. The chapter on regional anesthesia is clear and concise. The illustrations are exact and carefully described. This portion of the book is recommended to the obstetrician as well as the anesthesiologist.

IRVING M. PALLIN, M.D.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Franz Joseph Gall, Inventor of Phrenology, and His Collection. By Erwin H. Ackerknecht, M.D.; and Henri V. Vallois, M.D. Translated from the French by Claire St. Léon. Preface by John Z. Bowers, M.D. 8°, paper, 86 pp., with 7 illustrations, 13 tables and 2 plates. Madison: University of Wisconsin Medical School, 1956. (*Wisconsin Studies in Medical History.*) $1.50.

Neuropharmacology: Transactions of the Second Conference, May 25, 26, and 27, 1955, Princeton, New Jersey. Edited by Harold A. Abramson, M.D., research psychiatrist, Biological Laboratory, Cold Spring Harbor, New York, and assistant clinical professor of physiology, Columbia University College of Physicians and Surgeons. 8°, cloth, 328 pp., with 85 illustrations and 26 tables. New York: Josiah Macy, Jr. Foundation, 1956. $4.25.

Polysaccharides in Biology: Transactions of the First Conference, April 27, 28, and 29, 1955, Princeton, New Jersey. Edited by Georg F. Springer, M.D., William Pepper Laboratory of Clinical Medicine, Hospital of the University of Pennsylvania. 8°, cloth, 271 pp., with 31 illustrations and 22 tables. New York: Josiah Macy, Jr. Foundation, 1956. $5.00.

Clinical Studies in Psychiatry. By Harry Stack Sullivan, M.D. Edited by Helen Swick Perry, Mary Ladd Gawel and Martha Gibbon. With a foreword by Dexter M. Bullard, M.D. 8°, cloth, 386 pp. New York: W. W. Norton and Company, Incorporated, 1956. $5.50. (Prepared under the auspices of the William Alanson White Psychiatric Foundation Committee on Publication of Sullivan's Writings.)

Recent Advances in Pharmacology. By J. M. Robson, M.D., D.Sc., F.R.S.E., professor of pharmacology, Guy's Hospital Medical School, University of London; and C. A. Keele, M.D., F.R.C.P. (London), professor of pharmacology and therapeutics, Middlesex Hospital Medical School, University of London. Second edition. 8°, cloth, 501 pp., with 66 illustrations, 10 tables and a frontispiece. Boston: Little, Brown and Company, 1956. $8.00.

Essential Urology. By Fletcher H. Colby, M.D., consultant, Massachusetts General Hospital, urologic consultant, Lake-

ville State Sanatorium, Middleboro, and Lemuel Shattuck Hospital, Boston. Third edition. 8°, cloth, 656 pp., with 358 illustrations and 10 tables. Baltimore: The Williams and Wilkins Company, 1956. $8.00.

Essentials of Psychology. By Werner Wolff, professor of psychology, Bard College, Annandale-on-Hudson, New York. Second edition, revised and enlarged, of *What is Psychology?* 8°, cloth, 385 pp., with 92 illustrations. New York: Grune and Stratton, 1956. $6.50.

J.A.M.A. Clinical Abstracts of Diagnosis and Treatment. Abstracts selected by Noah D. Fabricant, M.D., editorial associate, *Journal of the American Medical Association.* 8°, cloth, 661 pp. New York: Intercontinental Medical Book Corporation with Grune and Stratton, Incorporated, 1956. $5.50. (Published with the approval of the Board of Trustees, American Medical Association.)

Proctology. By Harry E. Bacon, M.D., Sc.D., LL.D., F.R.S.M. (Lond.), professor of proctology and head, Department of Proctology, Temple University School of Medicine; Stuart T. Ross, M.D., F.A.P.S., F.I.C.S., attending proctologist, Nassau Hospital, Mineola, and Mercy Hospital, Rockville Centre, New York; and Porfirio Mayo Recio, M.D., M.Sc., F.P.C.S., F.I.C.S., assistant professor of surgery, College of Medicine, University of Philippines, and attending proctologic surgeon, Philippine General Hospital. 8°, cloth, 441 pp., with 228 illustrations, 31 tables and 5 colored plates. Philadelphia: J. B. Lippincott Company, 1956. $10.00.

An Introduction to Electrocardiography. By L. Schamroth, M.B., B.Ch. (Rand), M.R.C.P.E., F.R.F.P.S., University of Witwatersrand and General Hospital, Johannesburg. 8°, cloth, 60 pp., with 106 illustrations and 2 tables. Cape Town, South Africa: Juta and Company, Limited, 1956. Price 21/-.

Clinical Urology for General Practice. By Justin J. Cordonnier, M.D., professor of urology, Washington University School of Medicine, St. Louis, chief, Department of Urology, Barnes, St. Louis Children's, and allied hospitals, chief of urology, Washington University Clinics, and consultant in urology, United States Veterans Administration Hospital, St. Louis, Missouri. 4°, cloth, 252 pp., with 47 illustrations and 3 tables. St. Louis: The C. V. Mosby Company, 1956. $6.75.

The Treatment of Fractures. By Lorenz Böhler, M.D., director, Accident Hospital, Vienna, and professor of accident surgery, University of Vienna. Translated from the thirteenth German edition by Hans Tretter, Helen B. Luchini, Frank Kreuz, Otto A. Russe and Robert G. B. Bjornson. 8°, cloth, 1084 pp., with 1721 illustrations. New York: Grune and Stratton, 1956. $24.50.

Muscle Testing: Techniques of manual examination. By Lucille Daniels, M.A., associate professor and director of physical therapy, Department of Allied Medical Sciences, School of Medicine, Stanford University; Marian Williams, Ph.D., assistant professor of physical therapy, Stanford University; and Catherine Worthingham, Ph.D., director of professional education, The National Foundation for Infantile Paralysis, Incorporated. Second edition. 4°, paper, 176 pp., with format and test illustrations by Harold Black and anatomic drawings by Lorene Sigal. Philadelphia: W. B. Saunders Company, 1956. $4.00.

Clinical Urology. Vol. 1 and 2. By Oswald Swinney Lowsley, M.D., F.I.C.S., first director, Department of Urology (James Buchanan Brady Foundation), New York Hospital, and president and director, Oswald Swinney Lowsley Foundation, Incorporated, St. Clare's Hospital, New York City; and Thomas Joseph Kirwin, M.D., F.I.C.S., professor of urology, New York Medical College, director, Department of Urology, Flower and Fifth Avenue Hospitals, and director, Urological Department, Metropolitan and Bird S. Coler hospitals, New York City. Third edition. 4°, cloth, 1014 pp., with 599 illustrations and 7 colored plates drawn by William P. Didusch. Baltimore: The Williams and Wilkins Company, 1956. $32.50 per set.

Diagnostic Roentgenology. Edited by Ross Golden, M.D., visiting professor of radiology, University of California, Los Angeles. 4°, cloth, renewal pages for Vol. 1, 2 and 3, with 195 illustrations and 6 tables. Baltimore: The Williams and Wilkins Company, 1956. $15.00.

Dentistry: As I see it today. By A. Leroy Johnson, D.M.D., A.M., D.Sc. (Tufts, Rochester). With an introduction by Alan Gregg, M.D. 12°, cloth, 54 pp., with 1 chart. Boston: Little, Brown and Company, 1955. $2.50.

Alcoholism: Its psychology and cure. By Frederick B. Rea. 12°, cloth, 143 pp. New York: Philosophical Library, 1956. $3.50.

Current Therapy 1956: Latest approved methods of treatment for the practicing physician. Edited by Howard F. Conn, M.D. 4°, cloth, 632 pp., with tables. Philadelphia: W. B. Saunders Company, 1956. $11.00.

Blakiston's New Gould Medical Dictionary: A modern comprehensive dictionary of the terms used in all branches of medicine and allied sciences, including medical physics and chemistry, dentistry, pharmacy, nursing, veterinary medicine, zoology and botany, as well as medicolegal terms. Edited by Normand L. Hoerr, M.D., and Arthur Osol, Ph.D. Second edition. 4°, cloth, 1463 pp., with 252 illustrations on 45 plates, 129 in color and tables. New York: The Blakiston Division, McGraw-Hill Book Company, Incorporated, 1956. $11.50.

Hospitalization and Evacuation: Zone of interior. By Clarence McKittrick Smith. 4°, cloth, 503 pp., with illustrations, 18 tables and charts. Washington, D. C.: Office of the Chief of Military History, Department of the Army, 1956. $4.00. *(The Technical Services of the Medical Department, United States Army in World War II.)*

Anatomy for Surgeons: The thorax, abdomen, and pelvis. Vol. 2. By W. Henry Hollinshead, Ph.D., professor of anatomy, Mayo Foundation, University of Minnesota, and head, Section of Anatomy, Mayo Clinic, Rochester, Minnesota. 4°, cloth, 934 pp., with 1109 illustrations. New York: Paul B. Hoeber, Incorporated, 1956. $20.00.

A Pictorial History of Medicine. By Otto L. Bettmann, Ph.D., founder and director of the Bettmann Archive, New York City. With a foreword by Philip S. Hench, M.D., Mayo Clinic, Rochester, Minnesota. 4°, cloth, 318 pp., with illustrations. Springfield, Illinois: Charles C Thomas, 1956. $9.50.

Who Is Who in Allergology. Edited by Egon Bruun, M.D., Copenhagen. 4°, cloth. Copenhagen: Munksgaard, 1956.

(Distributed in the United States by Essential Books, Incorporated, Fair Lawn, New Jersey.) (Published under the auspices of the International Association of Allergology.)

The Neuroses in Clinical Practice. By Henry P. Laughlin, M.D., assistant clinical professor of psychiatry, George Washington University School of Medicine, head, Psychiatry and Neurology Division, Suburban Hospital, Bethesda, Maryland, and consultant in psychiatry, Walter Reed Army Medical Center. 8°, cloth, 802 pp., with 33 tables. Philadelphia: W. B. Saunders Company, 1956. $12.50.

Microbiology: With applications to nursing. By Catherine Jones Witton, M.A., associate professor of biology, Simmons College, Boston. Second edition. 8°, cloth, 620 pp., with illustrations and tables. New York: The Blakiston Division, McGraw-Hill Book Company, Incorporated, 1956. $6.00.

An Atlas of Regional Dermatology. By G. H. Percival, M.D., Ph.D., F.R.C.P.E., D.P.H., Grant Professor of Dermatology, University of Edinburgh, and physician, Skin Department, Royal Infirmary, Edinburgh; and T. C. Dodds, F.I.M.L.T., F.I.B.P., F.R.P.S., laboratory supervisor, Department of Pathology, University of Edinburgh, and head, Photomicrography Unit at Department of Pathology, University of Edinburgh. 8°, cloth, 264 pp., with 475 clinical subjects illustrated in full color. Baltimore: the Williams and Wilkins Company, 1955. $19.00.

Progress in Clinical Obstetrics and Gynaecology. By T. L. T. Lewis, M.B., B.Chir.(Camb.), F.R.C.S.(Eng.), M.R.C.O.G., obstetric surgeon, Guy's Hospital, and surgeon, Queen Charlotte's Maternity Hospital and Chelsea Hospital for Women. 8°, cloth, 594 pp., with 90 illustrations. Boston: Little, Brown and Company, 1956. $12.00.

Cerebral Palsy: Advances in understanding and care. By Viola E. Cardwell, R.N., P.T., M.A. 8°, cloth, 625 pp., with 81 illustrations. New York: Association for the Aid of Crippled Children, 1956. $5.00.

Lysergic Acid Diethylamide and Mescaline in Experimental Psychiatry: Proceedings of the annual meeting of the American Psychiatry Association, Atlantic City, May 12, 1955. Edited by Louis Cholden, M.D., assistant clinical professor of psychiatry, University of California School of Medicine, Los Angeles. 8°, cloth, 85 pp., with 12 illustrations. New York: Grune and Stratton, 1956. $3.00.

Their Mothers' Daughters. By Edward A. Strecker, M.D.; and Vincent T. Lathbury, M.D. 8°, cloth, 255 pp. Philadelphia: J. B. Lippincott Company, 1956. $3.75.

NONCLINICAL NOTES

AMERICAN ASSOCIATION OF BLOOD BANKS

At the ninth annual meeting of the American Association of Blood Banks, which met in Boston last month, with the Sixth Congress of the International Society of Blood Transfusion, Dr. Mark F. Lesses, of Boston, was elected district director.

AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS

The following officers were elected by the American College of Obstetricians and Gynecologists: president, Ralph E. Campbell, M.D., Madison, Wisconsin; president-elect, R. Gordon Douglas, New York City; vice-presidents, Norman F. Miller, M.D., Ann Arbor, Michigan; Duncan E. Reid, M.D., Boston; secretary, C. Paul Hodgkinson, M.D., Detroit, Michigan; assistant secretary, John C. Ullery, M.D., Columbus, Ohio; treasurer, Herbert E. Schmitz, M.D., Chicago.

NOTICES

BOSTON CITY HOSPITAL HOUSE OFFICERS' ASSOCIATION

The House Officers' Association of the Boston City Hospital announces the schedule of the remaining evening lecture series for October to be held in the New Cheever Amphitheater, Dowling Building, Boston City Hospital, October 16 and 23, at 7 p.m. The program is as follows:

October 16. Medical Writing as a Communication Skill. Dr. Joseph Garland, editor, *New England Journal of Medicine.*

October 23. Remarks on the Practical Management of Some Common Diseases. Dr. Marion Sulzberger, professor of dermatology and syphilology and chairman, Department of Dermatology, New York University Postgraduate Medical School.

All interested physicians and medical students are invited to attend.

WALTER E. FERNALD STATE SCHOOL

The twenty-first postgraduate seminar in pediatric neuropsychiatry, on clinical presentations and pathology of various forms of mental deficiency, will be held at the Research Laboratories, Walter E. Fernald State School, Trapelo Road, Waltham, Massachusetts, Wednesdays, October 17 and 31, November 14 and 28 and December 12, from 4:00 to 6:00 p.m.

Attendance will be limited to graduates and students of medicine and psychology.

Applications should be forwarded to the Research Department of the Walter E. Fernald State School, Box C, Waverley 78, Massachusetts.

ASSOCIATION ON ALCOHOLISM

A discussion and demonstration of the procedures of a typical alcoholism clinic will be the main feature of the fall meeting of the Professional Association on Alcoholism to be held at 22 The Fenway on October 24, 1956, at 8:15 p.m.

The subject of discussion will be "What Makes An Alcoholic Tick—A Demonstration by the Personnel of the Rhode Island Division of Alcoholism."

Further information may be obtained from the Boston Committee on Alcoholism, Incorporated, Room 525, 419 Boylston Street, Boston.

CARNEY HOSPITAL

A lecture will be held in the Lecture Hall at Carney Hospital on Monday, October 15, at 12:00 noon.

Dr. Allan M. Butler will speak on the subject "Safe and Simple Parenteral Fluid Therapy, Including the Preoperative and Postoperative Patient."

The luncheon will be held at 11:30 a.m.

NEW ENGLAND POSTGRADUATE ASSEMBLY

The fourteenth annual New England Postgraduate Assembly will be held at the Hotel Statler, Boston, October 30 and 31 and November 1. The program is as follows:

TUESDAY, OCTOBER 30, 1956

MORNING SESSION

MOTION PICTURES

8:30 (1) *Routine Anorectal and Sigmoidoscopic Examination with Differential Diagnosis* (Dr. Malcolm R. Hill, Los Angeles)
(2) *Diagnosis and Office Management of the Arthritides* (Dr. William B. Rawls, New York)

9:00 RECESS.

LECTURES

9:20 *Infertility and Reproductive Factors in Marriage Counsel.* Dr. John Rock, Clinical Professor of Gynecology, Emeritus, Harvard Medical School; Director, Rock Reproductive Study Center, Free Hospital for Women.

10:00 *The Differential Diagnosis and Management of Pulmonary Dyspnea.* Dr. George W. Wright, Cardio-respiratory Clinic, St. Luke's Hospital, Cleveland, Ohio.

10:40 RECESS. Coffee will be served in the exhibit area.

SYMPOSIA

11:00 (1) *Treatment of Parkinsonism.*
Moderator: Dr. Robert S. Schwab, Neurologist and Director of the EEG Laboratory, Massachusetts General Hospital; Assistant Clinical Professor of Neurology, Harvard Medical School.
Dr. Irving S. Cooper, Assistant Professor, Neurologic Surgery, New York University, Bellevue Medical Center; Director, Department of Neurologic Surgery, St. Barnabas Hospital, New York.
(2) *Alcoholism.*
Moderator: Dr. Robert P. Smith, Consultant Physician and Chairman, Medical Advisory Committee, Vermont Alcoholic Rehabilitation Commission, Burlington.
Dr. Robert Fleming, Director, Alcoholic Clinic, Peter Bent Brigham Hospital; member, Committee on Alcoholism, American Medical Association.
Dr. Maurice Victor, Clinical Associate in Neurology, Harvard Medical School; Assistant Neurologist, Massachusetts General Hospital.

12:00 RECESS.

LUNCHEON PANELS

12:30 (A) *Newer Drugs in the Treatment of Emotionally Disturbed Patients.*
Moderator: Dr. Mark D. Altschule, Assistant Clinical Professor of Medicine, Harvard University; Director, Internal Medicine and Research in Clinical Physiology, McLean Hospital; Associate, Thorndike Laboratories, Boston City Hospital; Visiting Physician, Beth Israel Hospital; Attending Physician, Boston V. A. Hospital.
Dr. Justin Hope, Senior Physician, New England Center Hospital; Chief of Psychiatry, New England Center Hospital; Research Professor of Psychiatry, Tufts University School of Medicine.
Dr. Harold F. Brown, Staff, Newton-Wellesley Hospital; Staff, Glover Memorial Hospital; Chief of Medicine, Brooks Hospital, 1953.
(B) *Orthopedic Problems in Childhood.*
Moderator: Dr. James M. Baty, Professor and Chairman of Department of Pediatrics, Tufts University School of Medicine; Physician-in-Chief, The Boston Floating Hospital.
Dr. William T. Green, Clinical Professor of Surgery, Harvard Medical School; Orthopedic Surgeon-in-Chief, Children's Medical Center, Peter Bent Brigham Hospital.
Dr. Arthur A. Thibodeau, Associate Professor of Orthopedics, Tufts University School of Medicine; Acting Chief of Surgery, New England Center Hospital; Chief of Orthopedics, New England Center Hospital.

AFTERNOON SESSION

AFTERNOON PANELS

2:35 (1) *Renal Failure.*
Moderator: Dr. Joseph M. Hayman, Professor of Medicine and Dean of Tufts University School of Medicine; Senior Physician, New England Center Hospital.
Dr. Arnold S. Relman, Associate Professor of Medicine, Boston University School of Medicine; Attending Physician, Massachusetts Memorial Hospitals.
Dr. William B. Schwartz, Jr., Associate Professor of Medicine, Tufts University School of Medicine; Physician, New England Center Hospital.
(2) *Peripheral Vascular Diseases.*
Moderator: Dr. Robert R. Linton, Assistant Clinical Professor of Surgery, Harvard Medical School.
Dr. Allan D. Callow, Assistant Professor of Surgery, Tufts University School of Medicine; Surgeon, New England Center Hospital.
Dr. Sanford Wessler, Associate in Medicine, Harvard Medical School; Associate in Medicine and Physician to the Vascular Clinic, Beth Israel Hospital.

3:50 RECESS.

4:10 CLINICAL-PATHOLOGICAL CONFERENCE
Discussers: Dr. George W. Wright.
Dr. Robert Tennant, Pathologist, Hartford Hospital, Hartford, Connecticut; Associate Clinical Professor of Pathology, Yale University.

5:00 RECESS.

WEDNESDAY, OCTOBER 31, 1956

MORNING SESSION

MOTION PICTURES

8:30 (1) *Anemia* (Dr. William Dameshek)
(2) *Principles of Fracture Reduction* (Veterans Administration)

9:00 RECESS.

LECTURES

9:20 *Hemorrhagic Disorders.* Dr. Kenneth M. Brinkhous, Professor of Pathology, School of Medicine, University of North Carolina.

10:00 *Is Progress Being Made in Cancer Research?* Dr. C. P. Rhoads, Director, Sloan-Kettering Institute; Scientific Director, Memorial Center; Professor of Pathology, Sloan-Kettering Division, Cornell University Medical College.

10:40 RECESS. Coffee will be served in exhibit area.

SYMPOSIA

11:00 (1) *Can Atherosclerosis Be Prevented?*
Moderator: Dr. Samuel Proger, Professor and Chairman of Department of Medicine, Tufts University School of Medicine; Chief-of-Medicine, New England Center Hospital.
Dr. Ancel Keys, Professor and Director, Lab-

oratory of Physiological Hygiene, University of Minnesota.
DR. HOWARD B. SPRAGUE, Lecturer on Medicine, Harvard Medical School; Board of Consultation, Massachusetts General Hospital; Chief of Staff, House of the Good Samaritan.
DR. FREDERICK J. STARE, Professor of Nutrition and Chairman of the Department of Nutrition, Harvard School of Public Health.

(2) *Hormonal Treatment of Breast Cancer.*
Moderator: DR. HENRY M. LEMON, Associate Professor of Medicine, Boston University School of Medicine.
DR. OLOF H. PEARSON, Associate Professor of Medicine, Cornell University Medical College; Associate, Sloan-Kettering Institute; Associate Attending Physician, Medical Service, Memorial Hospital and James Ewing Hospital, New York.
DR. ANDREW G. JESSIMAN, Henry E. Warren Fellow and Instructor in Surgery, Harvard Medical School; Junior Associate in Surgery and Cancer Co-ordinator, Peter Bent Brigham Hospital.

12:00 RECESS.

LUNCHEON PANELS

12:30 (C) *The Jaundiced Patient.*
Moderator: DR. PERRY J. CULVER, Assistant Physician, Massachusetts General Hospital; Associate in Medicine, Harvard Medical School.
DR. RICHARD B. CATTELL, Director, Lahey Clinic; Surgeon-in-Chief, New England Baptist Hospital; Surgeon, New England Deaconess Hospital.
DR. WILLIAM DAMESHEK, Professor of Medicine, Tufts University School of Medicine; Senior Physician and Chief of Hematology, New England Center Hospital.

12:30 (D) "CURBSTONE CONSULTATIONS."
2:15 RECESS.

AFTERNOON SESSION

AFTERNOON PANELS

2:35 (1) *New Practical Aspects of Cardiac Therapy.*
Moderator: DR. HARRY GOLD, Professor of Clinical Pharmacology, Cornell University.
DR. A. STONE FREEDBERG, Assistant Professor of Medicine, Harvard Medical School; Associate Director of Medical Research, Beth Israel Hospital.
DR. BERNARD LOWN, Junior Associate in Medicine, Peter Bent Brigham Hospital; Assistant in Medicine, Harvard Medical School.

(2) *Perinatal Perils.*
Moderator: DR. BENJAMIN TENNEY, Director, Obstetrics and Gynecology, Boston City Hospital; Clinical Professor of Obstetrics, Harvard Medical School.
DR. STEWART H. CLIFFORD, Assistant Clinical Professor of Pediatrics, Harvard Medical School; Pediatrician, Boston Lying-in Hospital; Chief of Premature Service, Children's Medical Center.
DR. JOHN F. SULLIVAN, Professor of Neurology, Tufts University School of Medicine; Neurologist-in-Chief, New England Center Hospital.

3:50 RECESS.
4:10 CLINICAL-PATHOLOGICAL CONFERENCE
Discussers: DR. HARRY GOLD, Professor of Clinical Pharmacology, Cornell University.
DR. JOSEPH PORTER, Pathologist, Maine Medical Center.

THURSDAY, NOVEMBER 1, 1956

MORNING SESSION

MOTION PICTURES

8:30 (1) *Myasthenia Gravis*
(Myasthenia Gravis Foundation)
(2) *Modern Concepts of Epilepsy*
(Dr. Francis Forester, Georgetown Medical School)
9:00 RECESS.

LECTURES

9:20 *The Place of Surgery in the Treatment of Cardiovascular Disease.* DR. CHARLES P. BAILEY, Professor of Thoracic Surgery, Hahnemann Hospital, Philadelphia, Pennsylvania.
10:00 *To What Extent Can Sulfonamides Orally Replace Insulin?* DR. ALEXANDER MARBLE, Clinical Associate in Medicine, Harvard Medical School.
10:40 RECESS. Coffee will be served in exhibit area.

SYMPOSIA

11:00 (1) *Long-Term Anticoagulant Therapy in the Ambulatory Patient.*
Moderator: DR. BENJAMIN ALEXANDER, Associate Professor of Medicine, Harvard Medical School; Associate Director of the Medical Service, Beth Israel Hospital.
DR. C. MILLER FISHER, Associate Neurologist, Massachusetts General Hospital; Assistant Professor of Neurology, Harvard Medical School.
DR. JAMES H. CURRENS, Assistant in Medicine, Massachusetts General Hospital; Associate Physician, Boston Lying-in Hospital; Consultant, Long Island Hospital.

(2) *Painful Shoulder.*
Moderator: DR. JOSEPH S. BARR, John B. and Buckminster Brown Clinical Professor of Orthopedic Surgery, Harvard Medical School; Chief of Orthopedic Service, Massachusetts General Hospital.
DR. THEODORE BAYLES, Clinical Associate in Medicine, Harvard Medical School; Visiting Physician and Director of Research, Robert Breck Brigham Hospital; Associate in Medicine, Peter Bent Brigham Hospital.
DR. J. LELAND SOSMAN, Radiologist, Robert Breck Brigham Hospital; Associate Radiologist, Peter Bent Brigham Hospital; Instructor in Radiology, Harvard Medical School.

12:00 RECESS.

LUNCHEON PANELS

12:30 (E) *Untoward Reactions to Drug and Antibiotic Therapy.*
Moderator: DR. FRANK P. FOSTER, Department of Internal Medicine, Lahey Clinic; Visiting Physician, New England Deaconess Hospital and New England Baptist Hospital.
DR. DALE G. FRIEND, Associate in Medicine, Harvard Medical School; Senior Associate in Medicine, Peter Bent Brigham Hospital.
DR. LOUIS WEINSTEIN, Associate Professor of Medicine, Boston University School of Medicine; Chief, Department of Infectious Diseases, Massachusetts Memorial Hospitals.
DR. JAMES F. PATTERSON, Assistant Professor of Medicine, Tufts University School of Medicine; Physician, New England Center Hospital.

12:30 (F) "CURBSTONE CONSULTATIONS."
2:15 RECESS.

AFTERNOON SESSION

AFTERNOON PANEL

2:35 *Ulcerative Colitis, Ileocolitis, and Ileitis.*
Moderator: DR. FRANZ INGELFINGER, Associate

Professor of Medicine, Boston University School of Medicine.

Dr. I. S. Ravdin, Chief of Surgical Services, University of Pennsylvania Hospital; John Rhea Barton Professor of Surgery, University of Pennsylvania Medical School.

Dr. Louis Zetzel, Clinical Associate in Medicine, Harvard Medical School; Chief, Gastrointestinal Clinic, Beth Israel Hospital; Consultant in Medicine to the First Army Medical Corps.

3:50 RECESS.

4:10 CLINICAL-PATHOLOGICAL CONFERENCE

Discussers: Dr. I. S. Ravdin.

Dr. George F. Meissner, Associate Pathologist, Rhode Island Hospital; Assistant Professor of Pathology, Tufts University School of Medicine.

NEW ENGLAND PEDIATRIC SOCIETY

The next meeting of the New England Pediatric Society will be held in the auditorium of the Jimmy Fund Building, 35 Binney Street, Boston, on Wednesday, October 24.

The scientific session will take place in the afternoon. Dr. Louis K. Diamond will act as chairman. The evening meeting will be held at Longwood Towers.

MASSACHUSETTS CONFERENCE ON SCHOOL HEALTH

The Massachusetts Conference on School Health, sponsored by the Committee on School Health, Massachusetts Medical Society, in co-operation with the Massachusetts School Physicians Association, Massachusetts Chapter of the American Academy of General Practice, Massachusetts Chapter of the American Academy of Pediatrics, Massachusetts Department of Public Health, Massachusetts Department of Mental Health, Massachusetts Department of Education and the Massachusetts Dental Society, will be held at the Hotel Statler, Boston, on Wednesday, October 17.

Program

9:00 a.m. Registration. Continuing throughout program. (Fee $1.00.)

9:45 a.m. Greetings from Howard F. Root, M.D., president of the Massachusetts Medical Society.

10:00 a.m. School Health in Action. Color and sound film produced for Oklahoma State Department of Health.

10:00 a.m. Panel discussion on the physician and the school, Harold C. Stuart, M.D., professor of maternal and child health, Harvard School of Public Health, moderator. Robert E. Archibald, M.D., deputy commissioner, Massachusetts Department of Public Health; Maurice M. Osborne, Jr., M.D., director of child health, Health Department, Brookline; Miss Elizabeth Stobo, R.N., formerly of Division of Nursing Education, Teachers College, Columbia University; Richard N. Anketell, superintendent of schools, Framingham; and Leon Sternfeld, M.D., commissioner of health, Cambridge.

12:30 p.m. Luncheon ($3.25), Commissioner John S. Desmond, Jr., Department of Education, Commonwealth of Massachusetts, presiding. Dental-Health Problems of School Children. James M. Dunning, D.D.S., chairman, Council on Dental Health, Massachusetts Dental Society.

2:15 p.m. Limitations of Visual and Auditory Tests. E. Porter Jewett, Jr., M.D., Worcester (visual), and M. Stuart Strong, M.D., Boston (auditory).

2:45 p.m. Supervised School-Physical-Education Program. Robert T. Berry, director of physical education, Springfield School Department.

3:15 p.m. Panel discussion on mental and physical health in the classroom, Warren T. Vaughan, Jr., M.D., assistant professor of mental health, Harvard School of Public Health, and director, Division of Mental Hygiene, Massachusetts Department of Public Health, moderator. Frank C. Chase, superintendent of schools, Gardner; and Richmond S. Paine, assistant pediatrician and assistant neurologist, Children's Medical Center, Boston.

4:15 p.m. Summation and Appraisal of Conference. Donald A. Dukelow, M.D., consultant, Bureau of Health Education, American Medical Association.

4:45 p.m. Closing remarks. Kenneth L. Maclachlan, M.D., Melrose, member, Committee on School Health, Massachusetts Medical Society.

THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS

The Fifth Annual Clinical Meeting of the American College of Obstetricians and Gynecologists will be held at the Palmer House, Chicago, November 7-9. Round-table discussions and breakfast conferences will be supplemented by panel discussions, formal papers and a new feature, "consultation hours," at which outstanding specialists will answer questions.

Entertainment has been arranged for the wives of the physicians attending the meeting. Further information may be obtained from Patricia Dorr, Public Relations, American College of Obstetricians and Gynecologists, 116 South Michigan, Chicago, Illinois.

AMERICAN COLLEGE OF CARDIOLOGY

The fifth interim meeting of the American College of Cardiology will be held at the Webster Hall Hotel, Pittsburgh, Pennsylvania, November 28-30.

The general topic for the meeting will be "Coronary-Artery Disease and Myocardial Infarction." The scientific sessions will feature four symposiums on diagnosis, recent trends in medical and surgical therapy, industrial and compensation aspects and rehabilitation and medicolegal problems.

Further information may be obtained from Dr. Phillip Reichart, Secretary, American College of Cardiology, Empire State Building, New York 1, New York.

AMERICAN COLLEGE OF CHEST PHYSICIANS AND THE OVERHOLT THORACIC CLINIC

There will be a combined meeting of the New England States Chapter of the American College of Chest Physicians and the Overholt Thoracic Clinic in the Joslin Auditorium of the New England Deaconess Hospital, Boston, on Wednesday, October 17, at 4 p.m.

Dr. Thomas K. Burnap will give a talk entitled "The Role of Assisted Ventilation in the Treatment of Chronic Pulmonary Disease."

All interested physicians are invited to attend.

SOCIETY MEETINGS AND CONFERENCES

October 11–31. Consultation Clinics for Crippled Children in Massachusetts. Page 626, issue of September 27.

October 12. American Society of Anesthesiologists. Page 490, issue of September 6.

October 12. New England Rheumatism Society. Page 489, issue of September 6.

October 12 and 13. International Cancer Cytology Congress. Page 104, issue of July 12.

October 12 and 13. American Rhinologic Society. Page 490, issue of September 6.

October 15. Carney Hospital. Page 728.

October 15–17. American College of Gastroenterology. Page 539, issue of September 13.

October 15–26. New York Academy of Medicine. Page 304, issue of August 9.

October 16. South End Medical Club. Page 675, issue of October 4, 1956.

October 16 and 23. Boston City Hospital House Officers' Association. Page 728.

October 17. Massachusetts Conference on School Health. Notice above.

October 17. Massachusetts Society of Examining Physicians. Page 584, issue of September 20.

October 17. American College of Chest Physicians and the Overholt Thoracic Clinic. Notice above.

October 17 and 31, November 14 and 28 and December 12. Walter E. Fernald State School. Page 728.

October 19 and December 14, 1956, and February and April, 1957. Massachusetts Society for Research in Psychiatry. Page 56, issue of July 5.

OCTOBER 24. New England Pediatric Society. Page 731.
OCTOBER 24. Association on Alcoholism. Page 728.
OCTOBER 29. University of Virginia. Page 627, issue of September 27.
OCTOBER 30 and 31 and NOVEMBER 1. New England Postgraduate Assembly, Boston. Page 729.
NOVEMBER 4–8. American Institute of Dental Medicine. Page 675, issue of October 4.
NOVEMBER 7–9. American College of Obstetricians and Gynecologists. Page 731.
NOVEMBER 12–16. American Public Health Association. Page 675, issue of October 4.
NOVEMBER 14–22. Pan-Pacific Surgical Association. Page 490, issue of September 6.
NOVEMBER 18–22. Pan American Medical Association. Page 490, issue of September 6.
NOVEMBER 28–30. American College of Cardiology. Page 731.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, OCTOBER 18

THURSDAY, OCTOBER 18

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Surgical Grand Rounds. Dr. John Spellman and staff. Saint Elizabeth's Hospital.
8:00–9:00 a.m. Medical Journal Club. Joslin Auditorium, New England Deaconess Hospital.
*8:45–9:45 a.m. Cardiac Grand Rounds. Yamins A, Beth Israel Hospital.
*9:00–10:00 a.m. Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*10:00–11:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Medical Grand Rounds. Dr. Sylvester McGinn and staff. Saint Elizabeth's Hospital.
*11:00 a.m.–12:00 m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*12:00 m. Clinicopathological Conference. Dr. Benjamin Castleman and associates. Pathology Amphitheater, Massachusetts General Hospital.
*12:15–1:15 p.m. Tumor Clinic. Dr. T. W. Botsford. Amphitheater, Peter Bent Brigham Hospital.
*3:00 p.m. Thoracic Conference. The Thoracic Service Presents Cases of Medical and Surgical Interest. Drs. Dwight E. Harken and Warren J. Taylor. Main Amphitheater, Peter Bent Brigham Hospital.

FRIDAY, OCTOBER 19

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:30 p.m. Medical Grand Rounds. Stearns Auditorium, New England Center Hospital.
*12:00 m. Pediatric Grand Rounds. Thorndike Amphitheater, Boston City Hospital.
*12:30–1:30 p.m. Surgical Grand Rounds. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*2:00–3:00 p.m. Pathology Conference. Dr. James Graham. Saint Elizabeth's Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Morton Street, Jamaica Plain.
*4:30 p.m. Neuroradiologic Conference. X-Ray Conference Room, New England Deaconess Hospital.

SATURDAY, OCTOBER 20

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*8:30–10:00 a.m. Surgical Grand Rounds. Drs. Charles G. Child, III, A. J. A. Campbell and staff. First (Tufts) Surgical Service, New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*9:00–10:00 a.m. Anesthesiology Conference. Dr. Benjamin Etsten. Anesthesia Laboratory, New England Center Hospital.
*9:30–11:00 a.m. Surgical House Officers' Conference. Second-Floor Conference Room, Carney Hospital, Dorchester.
*10:30 a.m. Teaching Ward Rounds. Ward South 2, Free Hospital for Women.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Hematology Conference. Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.

MONDAY, OCTOBER 22

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:30 p.m. Staff Conference. Child Psychiatry. By appointment. Conference Room (Burnham 7), Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Pediatric Clinicopathological Conference. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*12:00 m.–1:00 p.m. Endocrine Conference. Dr. Astwood. Stearns Auditorium, New England Center Hospital.
*12:00 m.–1:00 p.m. Tumor Conference. Dr. C. C. Lund and members of the Tumor Board. Dowling Amphitheater, Boston City Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. X-Ray Conference. Dr. William Carey. Saint Elizabeth's Hospital.
*3:00–4:00 p.m. Neuroradiologic Conference. Dr. Bertram Selverstone. Stearns Auditorium, New England Center Hospital.
*4:00 p.m. Clinicopathological Conference. Pathology Conference Room, Beth Israel Hospital.
*4:00–5:30 p.m. Anesthesiology Conference, Physical Principles Underlying Nitrous Oxide Anesthesia. Dr. Leroy D. Vandam. Surgical Conference Room, Peter Bent Brigham Hospital.
*4:00–5:30 p.m. Anesthesiology Conference. Dr. Benjamin Etsten. Stearns Auditorium, New England Center Hospital.
*5:00–6:30 p.m. Anesthesia Group of the Lahey Clinic. Joslin Auditorium, New England Deaconess Hospital.
*7:00–9:00 p.m. Slide Seminar in Pathology. Dr. Edward T. MacMahon. Stearns Auditorium, New England Center Hospital.
*7:00–9:00 p.m. Anesthesia Teaching Conference of Greater Boston. Coma — Diagnosis and Treatment. Dr. Hand. Auditorium, Jimmy Fund Building, Children's Medical Center, 35 Binney Street.

TUESDAY, OCTOBER 23

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical Grand Rounds. Pathology Conference Room, Carney Hospital, Dorchester.
*10:30 a.m. Medical Grand Rounds. Main Conference Room (Ground Floor), Lemuel Shattuck Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m.–1:00 p.m. Pediatric Grand Rounds. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Clinicopathological or Medicopathological Conference. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. X-Ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Hematology Conference. Dr. Mario Stefanini. Saint Elizabeth's Hospital.
*5:00 p.m. Surgical Journal Review. Mount Auburn Hospital, Cambridge.
*5:00–6:00 p.m. Service Meeting Followed by Clinical Conference (Medical, Surgical, Obstetric). Faulkner Hospital.

WEDNESDAY, OCTOBER 24

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. Deaconess A. New England Deaconess Hospital.
*8:00–9:00 a.m. Surgical Grand Rounds. Auditorium, Carney Hospital, Dorchester.
*9:00–10:00 a.m. Surgical Grand Rounds. Massachusetts Memorial Hospitals.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Orthopedic Grand Rounds. Bigelow Amphitheater, White 3A, Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Boston State Hospital Psychiatry Seminar. Progress in Therapy. Reception Building Auditorium, 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Roentgen Diagnostic Conference. 5th-floor teaching unit, Beth Israel Hospital.
*12:00 m.–1:00 p.m. Neurology, Neurosurgery and Psychiatry Conference. Drs. John F. Sullivan, Justin Hope and Bertram Selverstone. Stearns Auditorium, New England Center Hospital.
*12:00 m.–1:00 p.m. Pediatric Medical-Surgical Rounds. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*12:00 m.–1:00 p.m. Pediatric Clinicopathological Conference. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*12:15 p.m. Vascular Rounds. Drs. Edward A. Edwards and Chilton Crane, D-Main, Peter Bent Brigham Hospital.
*12:30–1:30 p.m. Weekly Staff Review of Autopsies. Dr. William A. Meissner. Joslin Auditorium, New England Deaconess Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*1:00 p.m. Massachusetts General Hospital Hand Clinic. The Clinics of the Massachusetts General Hospital.
*2:00 p.m. Rectal Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Pediatric Conference for Practitioners. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.
*4:00–6:00 p.m. Overholt Thoracic Conference. Joslin Auditorium, New England Deaconess Hospital.
*6:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*6:30 p.m. Lahey Clinic Lecture. Allergic Emergencies: Surgical and medical. Dr. John L. Fromer. Drug Poisoning. Dr. Albert F. Gigot. Joslin Auditorium, New England Deaconess Hospital.

*Open to the medical profession.